EXHIBIT A

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
AT CHARLESTON

IN RE: ETHICON, INC. PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION **This Document Relates to All Cases** **And** **Case No. 2:12-CV-04301**	**Master File No. 2:12-MD-02327** **MDL No. 2327** **JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**

DEFENDANTS' FIRST SET OF REQUESTS FOR ADMISSIONS TO PLAINTIFFS

Defendants Ethicon, Inc. and Johnson & Johnson (collectively, "Defendants"), pursuant to FED. R. CIV. P. 36, submit their first set of requests for admissions to Plaintiffs.

REQUESTS FOR ADMISSIONS

Notice of Claimed Investigational Exemption (IND #1688) - 1964

1. Admit that a genuine copy of Ethicon's Notice of Claimed Investigational Exemption for a New Drug for polypropylene sutures (IND #1688), dated March 25, 1964, is located at Bates numbered pages ETH.MESH.09625989 through 09626241.

Prolene Suture New Drug Application (NDA #16-374) – 1966-1969

2. Admit that a genuine copy of Ethicon's initial New Drug Application for Prolene polypropylene monofilament sutures ("Prolene sutures") (NDA #16-374) dated

January 17, 1966, is located at Bates numbered pages ETH.MESH.09625817 through 09625947, 09625962 through 09625973, and 09626242 through 09629458.

3. Admit that the document attached as Exhibit 1 and produced at Bates numbered pages ETH.MESH.09625731 through 09625737 is a genuine copy of the FDA's approval letter dated April 16, 1969, for NDA #16-374, Prolene sutures.

4. Admit that on April 16, 1969, the FDA approved Prolene sutures as "safe and effective for use as recommended in the submitted labeling."

5. Admit that the FDA approved the packaging, labels, and labeling submitted by Ethicon as part of NDA #16-374.

Supplements to NDA #16-374 – 1970-1990

6. For each of the supplements to NDA #16-374 listed in Exhibit 2, admit that a genuine copy of Ethicon's application for the supplement (and any amendments to it) is located at the Bates numbered pages listed under the "Application" column.

7. For each of the supplements to NDA #16-374 listed in Exhibit 2, admit that the applications were submitted to the FDA on or about the date(s) identified in Exhibit 2 under the "Application Date(s)" column.

1970

8. Admit that the document attached as Exhibit 3 and produced at Bates numbered page ETH.MESH.09629720 is a genuine copy of the FDA's approval letter dated May 8, 1970, for Supplemental NDA #16-374/S-001.

9. Admit that the FDA approved Supplemental NDA #16-374/S-001 on May 8, 1970.

10. Admit that the document attached as Exhibit 4 and produced at Bates numbered page ETH.MESH.09629714 is a genuine copy of the FDA's amended approval letter dated June 29, 1970, for Supplemental NDA #16-374/S-001.

11. Admit that the FDA amended its approval of Supplemental NDA #16-374/S-001 on June 29, 1970.

1972

12. Admit that the document attached as Exhibit 5 and produced at Bates numbered page ETH.MESH.09630681 is a genuine copy of the FDA's approval letter dated August 17, 1972, for Supplemental NDA #16-374/S-002.

13. Admit that the FDA approved Supplemental NDA #16-374/S-002 as amended on August 17, 1972.

14. Admit that the document attached as Exhibit 6 and produced at Bates numbered page ETH.MESH. 09630683 is a genuine copy of the FDA's approval letter dated August 17, 1972, for Supplemental NDA #16-374/S-003.

15. Admit that the FDA approved Supplemental NDA #16-374/S-003 on August 17, 1972.

1973

16. Admit that the document attached as Exhibit 7 and produced at ETH.MESH.09630649 is a genuine copy of an April 26, 1973, letter from the FDA to Ethicon.

17. Admit that in Exhibit 7 the FDA recommended the addition of the following language to the IFU: "[I]n order to furnish adequate information for the safe use of the drug: transitory local inflammatory reactions have been reported."

18. Admit that the document attached as Exhibit 8 and produced at Bates numbered page ETH.MESH. 09630640 is a genuine copy of the FDA's approval letter dated June 26, 1973, for Supplemental NDA #16-374/S-005.

19. Admit that the FDA approved Supplemental NDA #16-374/S-005 as changed on June 26, 1973.

20. Admit that the document attached as Exhibit 9 and produced at Bates numbered page ETH.MESH. 09630742 is a genuine copy of the FDA's approval letter dated September 10, 1973, for Supplemental NDA #16-374/S-004.

21. Admit that the FDA approved Supplemental NDA #16-374/S-004 on September 10, 1973.

1974

22. Admit that the document attached as Exhibit 10 and produced at Bates numbered page ETH.MESH. 09630944 is a genuine copy of the FDA's approval letter dated March 1, 1974, for Supplemental NDA #16-374/S-006.

23. Admit that the FDA approved Supplemental NDA #16-374/S-006 on March 1, 1974.

24. Admit that the document attached as Exhibit 11 and produced at Bates numbered page ETH.MESH. 09630985 is a genuine copy of the FDA's approval letter dated November 18, 1974, for Supplemental NDA #16-374/S-007.

25. Admit that the FDA approved Supplemental NDA #16-374/S-007 on November 18, 1974.

1975

26. Admit that the document attached as Exhibit 12 and produced at Bates numbered page ETH.MESH.09631401 is a genuine copy of the FDA's approval letter dated January 16, 1975, for Supplemental NDA #16-374/S-008.

27. Admit that the FDA approved Supplemental NDA #16-374/S-008 on January 16, 1975.

28. Admit that the document attached as Exhibit 13 and produced at Bates numbered page ETH.MESH.09631463 is a genuine copy of the FDA's approval letter dated June 4, 1975, for Supplemental NDA #16-374/S-010.

29. Admit that the FDA approved Supplemental NDA #16-374/S-010 on June 4, 1975.

30. Admit that the document attached as Exhibit 14 and produced at Bates numbered page ETH.MESH.09631174 is a genuine copy of the FDA's approval letter dated September 22, 1975, for Supplemental NDA #16-374/S-009.

31. Admit that the FDA approved Supplemental NDA #16-374/S-009 as amended on September 22, 1975.

1976

32. Admit that the document attached as Exhibit 15 and produced at Bates numbered page ETH.MESH.09631713 is a genuine copy of the FDA's approval letter dated October 22, 1976, for Supplemental NDA #16-374/S-011.

33. Admit that the FDA approved Supplemental NDA #16-374/S-011 on October 22, 1976.

1978

34. Admit that the document attached as Exhibit 16 and produced at Bates numbered page ETH.MESH.09632315 is a genuine copy of the FDA's approval letter dated May 12, 1978, for Supplemental NDA #16-374/S-014.

35. Admit that the FDA approved Supplemental NDA #16-374/S-014 on May 12, 1978.

36. Admit that the document attached as Exhibit 17 and produced at Bates numbered page ETH.MESH.09632331 is a genuine copy of the FDA's approval letter dated December 20, 1978, for Supplemental NDA #16-374/S-015.

37. Admit that the FDA approved Supplemental NDA #16-374/S-015 on December 20, 1978.

1979

38. Admit that the document attached as Exhibit 18 and produced at Bates numbered page ETH.MESH.09632606 is a genuine copy of the FDA's approval letter dated April 9, 1979, for Supplemental NDA #16-374/S-016.

39. Admit that the FDA approved Supplemental NDA #16-374/S-016 as amended on April 9, 1979.

40. Admit that the document attached as Exhibit 19 and produced at Bates numbered page ETH.MESH.09632774 is a genuine copy of the FDA's approval letter dated May 18, 1979, for Supplemental NDA #16-374/S-018.

41. Admit that the FDA approved Supplemental NDA #16-374/S-018 on May 18, 1979.

42. Admit that the document attached as Exhibit 20 and produced at Bates numbered page ETH.MESH.09632959 is a genuine copy of the FDA's approval letter dated December 6, 1979, for Supplemental NDA #16-374/S-019.

43. Admit that the FDA approved Supplemental NDA #16-374/S-019 on December 6, 1979.

1980

44. Admit that the document attached as Exhibit 21 and produced at Bates numbered page ETH.MESH.09632673 is a genuine copy of the FDA's approval letter dated January 4, 1980, for Supplemental NDA #16-374/S-017.

45. Admit that the FDA approved Supplemental NDA #16-374/S-017 as amended on January 4, 1980.

46. Admit that the document attached as Exhibit 22 and produced at Bates numbered page ETH.MESH.09632861 is a genuine copy of the FDA's approval letter dated April 23, 1980, for Supplemental NDA #16-374/S-012.

47. Admit that the FDA approved Supplemental NDA #16-374/S-012 as amended on April 23, 1980.

48. Admit that the document attached as Exhibit 23 and produced at Bates numbered page ETH.MESH.09632899 is a genuine copy of the FDA's approval letter dated April 23, 1980, for Supplemental NDA #16-374/S-013.

49. Admit that the FDA approved Supplemental NDA #16-374/S-013 as amended on April 23, 1980.

50. Admit that the document attached as Exhibit 24 and produced at Bates numbered page ETH.MESH.09632978 is a genuine copy of the FDA's approval letter dated May 2, 1980, for Supplemental NDA #16-374/S-020.

51. Admit that the FDA approved Supplemental NDA #16-374/S-020 on May 2, 1980.

52. Admit that the document attached as Exhibit 25 and produced at Bates numbered page ETH.MESH.09633026 is a genuine copy of the FDA's approval letter dated December 17, 1980, for Supplemental NDA #16-374/S-1.

53. Admit that the FDA approved Supplemental NDA #16-374/S-1 on December 17, 1980.

1981

54. Admit that the document attached as Exhibit 26 and produced at Bates numbered pages ETH.MESH.09633003 through 09633004 is a genuine copy of the FDA's approval letter dated January 6, 1981, for Supplemental NDA #16-374/S-021.

55. Admit that the FDA approved Supplemental NDA #16-374/S-021 on January 6, 1981.

56. Admit that the document attached as Exhibit 27 and produced at Bates numbered page ETH.MESH.09633211 is a genuine copy of the FDA's approval letter dated January 14, 1981, for Supplemental NDA #16-374/S-2.

57. Admit that the FDA approved Supplemental NDA #16-374/S-2 on January 14, 1981.

1983

58. Admit that the document attached as Exhibit 28 and produced at Bates numbered pages ETH.MESH.09633361 through 09633362 is a genuine copy of the FDA's approval letter dated April 7, 1983, for Supplemental NDA #16-374/S26.

59. Admit that the FDA approved Supplemental NDA #16-374/S26 on April 7, 1983.

1984

60. Admit that the document attached as Exhibit 29 and produced at Bates numbered pages ETH.MESH.09633425 through 09633426 is a genuine copy of the FDA's approval letter dated March 12, 1984, for Supplemental NDA #16-374/S27.

61. Admit that the FDA approved Supplemental NDA #16-374/S27 on March 12, 1984.

1985

62. Admit that the document attached as Exhibit 30 and produced at Bates numbered pages ETH.MESH.09633444 through 09633446 is a genuine copy of the FDA's approval letter dated June 10, 1985, for Supplemental NDA #16-374/S28.

63. Admit that the FDA approved Supplemental NDA #16-374/S28 as amended on June 10, 1985.

1986

64. Admit that the document attached as Exhibit 31 and produced at Bates numbered pages ETH.MESH.09633998 through 09634005 is a genuine copy of the FDA's approval letter dated January 23, 1986, for Supplemental NDA #16-374/S29.

65. Admit that the FDA approved Supplemental NDA #16-374/S29 on January 23, 1986.

66. Admit that the document attached as Exhibit 32 and produced as Bates numbered pages ETH.MESH.09634080 through ETH.MESH.09634081 is a genuine copy of Section 6 of Ethicon's Annual Experience Report for PROLENE polypropylene suture covering the period from April 16, 1985 through April 15, 1986

67. Admit that in 1986, Ethicon reported to the FDA that 1.58 million dozen sutures had been sold within the past 12 months, as stated in the document attached as Exhibit 32 and produced as ETH.MESH.09634081.

68. Admit that the document attached as Exhibit 33 and produced at Bates numbered pages ETH.MESH.09634020 through 09634023 is a genuine copy of the FDA's approval letter dated May 23, 1986, for Supplemental NDA #16-374/S30.

69. Admit that the FDA approved Supplemental NDA #16-374/S30 on May 23, 1986.

70. Admit that the document attached as Exhibit 34 and produced at Bates numbered page ETH.MESH.09634106 is a genuine copy of the FDA's approval letter dated December 3, 1986, for Supplemental NDA #16-374/S31.

71. Admit that the FDA approved Supplemental NDA #16-374/S31 on December 3, 1986.

1987

72. Admit that the document attached as Exhibit 35 and produced at Bates numbered pages ETH.MESH.09634185 through 09634187 is a genuine copy of the FDA's approval letter dated August 28, 1987, for Supplemental NDA #16-374/S33.

73. Admit that the FDA approved Supplemental NDA #16-374/S33 on August 28, 1987.

1988

74. Admit that the document attached as Exhibit 36 and produced at Bates numbered pages ETH.MESH.09634299 through 09634303 is a genuine copy of the FDA's approval letter dated October 7, 1988, for Supplemental NDA #16-374/S34.

75. Admit that the document attached as Exhibit 37 and produced at Bates numbered page ETH.MESH.09634318 is a genuine copy of proposed changes to the package insert for Prolene polypropylene sutures that Ethicon submitted to the FDA as part of NDA #16-374/S34.

76. Admit that the proposed changes in NDA #16-374/S34 included labeling that warned of a "minimal, transient acute inflammatory reaction," and that it is not "subject to degradation or weakening by the action of tissue enzymes."

77. Admit that the proposed changes in NDA #16-374/S34 included labeling that said the material "resists involvement in infection."

78. Admit that the FDA approved Supplemental NDA #16-374/S34 on October 7, 1988.

1990

79. Admit that the document attached as Exhibit 38 and produced at Bates numbered pages ETH.MESH.09634354 through 09634356 is a genuine copy of the FDA's approval letter dated March 20, 1990, for Supplemental NDA #16-374/S35.

80. Admit that the FDA approved Supplemental NDA #16-374/S35 on March 20, 1990.

Prolene Suture Studies

81. Admit that the document produced at Bates numbered pages ETH.MESH.09626038 through 09626039 is a genuine copy of part of Ethicon's IND #1688, containing Usher, F.C., *Hernia Repair with Knitted Polypropylene Mesh*, Surgery, Gynecology & Obstetrics, Vol. 117, No. 2 (1963), submitted to the FDA as part of IND #1688.

82. Admit that the document produced at Bates numbered page ETH.MESH.09629996 is a genuine copy of part of Ethicon's Fourth Quarterly Progress Report for NDA #16-374, containing an abstract of Morgan, J.E., *A Sling Operation Using Marlex Polypropylene Mesh for Treatment of Recurrent Stress Incontience*, Vol. 106, No. 3, pages 369–77 (1970), submitted to the FDA on April 24, 1970.

83. Admit that the documents produced at Bates numbered pages ETH.MESH.09634276 and ETH.MESH.09634282 through 09634283 are a genuine copy of part of Ethicon's 1988 to 1989 periodic report for NDA #16-374, containing an abstract of Kersey, J. et al., *A Further Assessment of the Gauze Hammock Sling Operation in the Treatment of Stress Incontinence*, British J. Obstet. Gynaecol., 95(4):382–385 (1988), submitted to the FDA on June 28, 1989.

84. Admit that the document identified in Number 83 also contains an abstract of Gittes, R.F. & Foreman, R., *Transcutaneous Incorporation of Nonabsorbable Monofilament Sutures*, Surg. Gynecol.,Obstet., 166(6):545–548 (1988) submitted to the FDA on June 28, 1989.

Reclassification Order

85. Admit that from 1969 until the passage of the 1976 Medical Device Amendments, the FDA regulated Prolene polypropylene monofilament sutures as a drug.

86. Admit that, following the 1976 Medical Device Amendments enactment, the FDA regulated Prolene sutures as a Class III medical device.

87. Admit that the document attached as Exhibit 39 and produced at Bates numbered pages ETH.MESH.09634664 through 09634688 is a genuine copy of a July 5, 1990, FDA order.

88. Admit that according to Exhibit 39, the FDA reclassified nonabsorbable polypropylene surgical sutures from a Class III medical device to a Class II medical device with a low priority for the development of a performance standard.

89. Admit that the document attached as Exhibit 40 and produced at Bates numbered pages ETH.MESH.09634662 through 09634663 is a genuine copy of a letter from the FDA to Ethicon dated October 12, 1990, regarding the FDA's decision to reclassify polypropylene sutures as a Class II medical device.

90. Admit that on October 12, 1990, the FDA notified Ethicon that it reclassified PROLENE polypropylene sutures as a Class II medical device.

510(k) Submissions

Modified PROLENE Mesh - 1996

91. Admit that a genuine copy of Ethicon's 510(k) Premarket Notification dated June 25, 1996, for Modified PROLENE polypropylene mesh nonabsorbable synthetic surgical mesh ("Modified PROLENE 510(k)") is located at Bates numbered pages ETH.MESH.05217103 through 05217144.

92. Admit that a genuine copy of FDA's receipt letter to Ethicon concerning the Modified PROLENE 510(k) (K962530) is located at Bates numbered pages ETH.MESH.05217101 through 05217102.

93. Admit that a genuine copy of Section I ("Modified Device and Description") of Ethicon's Modified PROLENE 510(k) is attached as Exhibit 41 and located at Bates numbered pages ETH.MESH.05217110 through 05217111.

94. Admit that Ethicon's Modified PROLENE 510(k) states, in part, at ETH.MESH. 05217111 that "Modified PROLENE mesh is constructed of knitted filaments of extruded polypropylene identical in composition to that used in PROLENE* polypropylene suture nonabsorbable surgical sutures, U.S.P."

95. Admit that Ethicon's Modified PROLENE 510(k) states, in part, at ETH.MESH. 05217110 that the predicate device for Modified PROLENE mesh is "a preamendment device PROLENE polypropylene mesh nonabsorbable synthetic surgical mesh."

96. Admit that a genuine copy of the FDA's Clearance Letter for Ethicon's Modified PROLENE 510(k) dated August 9, 1996, is attached as Exhibit 42 and located at Bates numbered pages ETH.MESH.05217098 through 05217100.

97. Admit that the FDA cleared Ethicon's 510(k) submission for Modified PROLENE on August 9, 1996.

TVT - 1998

98. Admit that a genuine copy of Ethicon's 510(k) Premarket Notification dated October 29, 1997, for the Tension Free Vaginal Tape (TVT) System (K974098) ("TVT 510(k)") is located at Bates numbered pages ETH.MESH.08476210 through 08476342 and ETH.MESH.10040062 through 10040065.

99. Admit that a genuine copy of Section I ("New Device and Description") of Ethicon's TVT 510(k) is attached as Exhibit 43 and located at Bates numbered pages ETH.MESH.08476243 through 08476245.

100. Admit that the TVT 510(k) states that polypropylene mesh used in the Tension Free Vaginal Tape (TVT) System (K974098) "is the same Polypropylene mesh that is used to fabricate PROLENE polypropylene mesh," as stated in ETH.MESH.08476244.

101. Admit that the TVT 510(k) states that polypropylene strands used to fabricate PROLENE mesh are the "same strands used to fabricate PROLENE Polypropylene Nonabsorbable Surgical Suture (NDA/PMA #16-374)," as stated in ETH.MESH.08476244.

102. Admit that the PROLENE polypropylene mesh is the only part of the TVT System's device intended to be left in a patient's body following a TVT surgical procedure.

103. Admit that a genuine copy of the FDA's Clearance Letter for Ethicon's TVT 510(k) dated January 28, 1998, is attached as Exhibit 44 and located at Bates numbered pages ETH.MESH.08476211 through 08476213.

104. Admit that the FDA cleared Ethicon's 510(k) submission for TVT on January 28, 1998.

105. Admit that FDA has never rescinded its clearance of the 510(k) premarket notification for the Tension Free Vaginal Tape (TVT) System (K974098).

106. Admit that FDA has never rescinded the 510(k) premarket notification for the Tension Free Vaginal Tape (TVT) System (K974098).

107. Admit that the FDA has never issued a Warning Letter to Ethicon, Inc. regarding the Tension Free Vaginal Tape (TVT) System (K974098).

108. Admit that the FDA has never issued a Warning Letter to Johnson & Johnson regarding the Tension Free Vaginal Tape (TVT) System (K974098).

TVT-AA/Blue - 2001

109. Admit that a genuine copy of Ethicon's 510(k) Premarket Notification dated August 9, 2001, for the Modified TVT-Blue System, with Accessory TVT-AA (K012628) ("Modified TVT-Blue 510(k)") is located at Bates numbered pages ETH.MESH.10039072 through 10039200.

110. Admit that a genuine copy of Section I ("Modified Device and Description") of Ethicon's Modified TVT-Blue 510(k) is attached as Exhibit 45 and located at Bates numbered pages ETH.MESH.10039090 through 10039093.

111. Admit that, according to the Modified TVT-Blue 510(k), the Modified TVT-Blue System, with Accessory TVT-AA (K012628) ("TVT Blue") "is a modification of the currently marketed TVT device and accessories covered under 510(k) (K974098) cleared January 28, 1998" as stated in ETH.MESH.10039090.

112. Admit that, according to the Modified TVT-Blue 510(k), the TVT Blue "contains the same blue pigmented polypropylene monofilaments as the currently cleared

PROLENE* soft Polypropylene Mesh K001122 cleared on May 23, 2000" as stated in ETH.MESH.10039090.

113. Admit that, according to the Modified TVT-Blue 510(k), the TVT Blue is distinguished, in part, from the TVT system "by the inclusion of blue pigmented polypropylene fibers (approximately 50%) interwoven in the same manner as the current unpigmented TVT device," and that the "blue pigmented monofilaments are made from the same unpigmented polypropylene fibers colored with blue pigment [Phthalocyaninato(2-)] copper," as stated in ETH.MESH.10039090.

114. Admit that, according to the Modified TVT-Blue 510(k), the TVT Blue "is a sterile single-use device that is composed of one piece of approximately 50% unpigmented and 50% pigmented blue [Phthalocyaninato(2-) copper], (Colour index Number 74160) polypropylene mesh," and that "this is the same Polypropylene Mesh that is used to fabricate PROLENE* Soft Polypropylene mesh (K001122) and PROLENE* Polypropylene Mesh (K962530)," as stated in ETH.MESH.10039092.

115. Admit that, according to the Modified TVT-Blue 510(k), the "PROLENE mesh is fabricated from polypropylene strands of clear and clear/blue pigmented polypropylene fiber," and that "these same strands are used to fabricate PROLENE* Polypropylene Nonabsorbable Surgical Suture, undyed of blue pigment, (NDA;PMA #16-374) manufactured and marketed by ETHICON, Inc." as stated in ETH.MESH.10039092.

116. Admit that a genuine copy of the FDA's Clearance Letter for Ethicon's Modified TVT-Blue 510(k) submission, dated October 26, 2001, is attached as Exhibit 46 and located at Bates numbered pages ETH.MESH.10039077 through 10039079.

117. Admit that the FDA cleared Ethicon's 510(k) submission for the Modified TVT-Blue System on October 26, 2001.

118. Admit that the PROLENE polypropylene mesh is the only part of the Modified TVT-Blue System intended to be left in a patient's body following a TVT surgical procedure.

119. Admit that FDA has never rescinded its clearance of the Modified TVT Blue 510(k) (K012628).

120. Admit that FDA has never rescinded the Modified TVT Blue 510(k) (K012628).

121. Admit that the FDA has never issued a Warning Letter to Ethicon, Inc. regarding the TVT Blue device (K012628).

122. Admit that the FDA has never issued a Warning Letter to Johnson & Johnson regarding the TVT Blue device (K012628).

TVT-O - 2003

123. Admit that a genuine copy of Ethicon's 510(k) Premarket Notification dated December 8, 2003, for the GYNECARE TVT Obturator Device (K033568) ("TVT-O 510(k)") is located at Bates numbered pages ETH.MESH.07876926 through 07877006 and ETH.MESH.10039201 through 10039204.

124. Admit that a genuine copy of Section I ("Modified Device and Description") of Ethicon's TVT-O 510(k) is attached as Exhibit 47 and located at Bates numbered pages ETH.MESH.07876943 through 07876945.

125. Admit that, according to the TVT-O 510(k), the predicate device for the GYNECARE TVT Obturator Device "is a modification of the currently marketed GYNECARE TVT device covered under 510(k) K974098 cleared January 28, 1998" and "contains the

same blue pigmented polypropylene monofilaments as the currently cleared TVT Blue with Abdominal Guides K012628 cleared on October 26, 2001," as stated in ETH.MESH.07876943.

126. Admit that a genuine copy of the FDA's Clearance Letter for Ethicon's TVT-O 510(k) submission, dated December 8, 2003, is attached as Exhibit 48 and located at Bates numbered pages ETH.MESH.07876929 through 07876931.

127. Admit that the FDA cleared Ethicon's TVT-O 510(k) submission on December 8, 2003.

128. Admit that the PROLENE polypropylene mesh is the only part of the device intended to be left in a patient's body following a GYNECARE TVT Obturator surgical procedure.

129. Admit that FDA has never rescinded its clearance of the 510(k) premarket notification for the GYNECARE TVT Obturator Device (K033568).

130. Admit that FDA has never rescinded the 510(k) premarket notification for the GYNECARE TVT Obturator Device (K033568).

131. Admit that the FDA has never issued a Warning Letter to Ethicon, Inc. regarding the GYNECARE TVT Obturator Device (K033568).

132. Admit that the FDA has never issued a Warning Letter to Johnson & Johnson regarding the GYNECARE TVT Obturator Device (K033568).

Updated Clearance - 2012

133. Admit that a genuine copy of the FDA's updated clearance letter for Ethicon's TVT 510(k) submission (K974098), dated September 28, 2012, is attached as Exhibit 49 and located at Bates numbered pages ETH.MESH. 10040062 through10040065.

134. Admit that the FDA issued an updated clearance letter for the TVT System on September 28, 2012.

135. Admit that a genuine copy of the FDA's updated clearance letter for Ethicon's Modified TVT-Blue 510(k) submission (K012628), dated September 28, 2012, is attached as Exhibit 50 and located at Bates numbered pages ETH.MESH. 10039072 through 10039074.

136. Admit that the FDA issued an updated clearance letter for the TVT-Blue System on September 28, 2012.

137. Admit that a genuine copy of the FDA's updated clearance letter for Ethicon's TVT-O 510(k) submission (K033568), dated September 28, 2012, is attached as Exhibit 51 and located at Bates numbered pages ETH.MESH. 10039201 through 10039204.

138. Admit that the FDA issued an updated clearance letter for the TVT-O Device on September 28, 2012.

Respectfully submitted,
ETHICON, INC. AND
JOHNSON & JOHNSON

/s/ David B. Thomas
David B. Thomas (W. Va. Bar No. 3731)
Thomas Combs & Spann, PLLC
300 Summers Street, Suite 1380
P.O. Box 3824
Charleston, WV 23558-3824
(304) 414-1800

/s/ Christy D. Jones
Christy D. Jones
Butler, Snow, O'Mara, Stevens & Cannada, PLLC
1020 Highland Colony Parkway
Suite 1400 (39157)

P.O. Box 6010
Ridgeland, MS 39158-6010
(601) 985-4523

Exhibit Index

Exhibit 1

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
CONSUMER PROTECTION AND ENVIRONMENTAL HEALTH SERVICE
WASHINGTON, D.C. 20204

FOOD AND DRUG ADMINISTRATION

APR 16 1969

NDA 16-374

Xerox to: Dr. C. Artandi
Mr. A. J. Abbruzze
Mr. D. Collins
Mr. R. B. Sellars
Mr. S. Smoyer
Dr. A. W. Ulin

4/18/69

CERTIFIED AIR MAIL

Ethicon, Inc.
Attention: Mr. A. J. Bee
Somerville, New Jersey 08876

Gentlemen:

This acknowledges the receipt on February 6, 1969 of your communication dated February 5, 1969 enclosing printed labeling pursuant to your new drug application for "Prolene Polypropylene Suture (Nonabsorbable Surgical Suture U.S.P., Type B)".

We also acknowledge receipt of your additional communication dated March 3, 1969. Also those dated March 3 and March 14, 1969 enclosing revised printed labeling.

The application was filed on March 17, 1969.

We have completed the review of this application as amended and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the application is approved.

The enclosures summarize the conditions relating to the approval of this application.

Please submit two market packages of the drug when available.

Sincerely yours,

B. H. Minchew, M.D.
Acting Director
Bureau of Medicine

Enclosures
Records and Reports Requirement (Reg. 130.13)
Conditions of Approval of NDA

RECEIVED
APR 1 8 1969
R. J. SEMPLE

With the approval of your new drug application the following information should be submitted concerning any continuing clinical investigations and the disposition of the drugs supplied for investigational use of this product as provided for in your IND(s):

(1) Whether each clinical investigator has been informed that a new drug application has been approved and whether he has been supplied copies of the approved labeling;

(2) A statement as to which of the clinical investigations are continuing, showing whether or not the study involves use of the drug under conditions other than those covered by the approved labeling;

(3) The disposition of any unused drugs supplied for investigational use that are not intended for continuing investigation or use under the conditions covered by the approved labeling.

Reports of any continuing studies should be submitted as progress reports to your Notice of Claimed Investigational Exemption. Data submitted to the new drug application under the records and reports requirement may be included in the progress report by reference.

In the event you initiate additional clinical studies involving use of the drug under conditions not covered by the approved labeling in the new drug application, it will be necessary, of course, that we be notified. This may be in the form of a separate Notice or an amendment to your IND(s). Information in the discontinued Notice may also be included by specific reference.

Records and Reports Requirement
(21 CFR 130.13)

130.13 Records and reports concerning experience on drugs for which an approval is in effect.

(a) On receiving notification that an application for a new drug is approved, the applicant shall establish and maintain records and make reports that are necessary to facilitate a determination whether there may be grounds for invoking section 505(e) of the Act to suspend or withdraw approval of the application, including adequately organized and indexed files containing full reports or any of the following kinds of information, pertinent to the safety or effectiveness of the drug or the adequacy of the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of the drug to assure and preserve its identity, strength, quality, and purity, that has not previously been submitted as part of his application for the drug and which is received or otherwise obtained by him from any source:

(1) Unpublished reports of clinical experience, studies, investigations, and tests conducted by the applicant or reported to him by any person involving the drug that is the subject of the application and related drugs, and reports in the scientific literature involving the drug that is the subject of the application. An adequate summary and bibliography of reports in the scientific literature will ordinarily suffice. (The applicant must identify at the time of each report submission each drug he considers related to the subject drug.)

(2) Unpublished reports of animal experience, studies, investigations, and tests conducted by the applicant or reported to him by any person involving the drug that is the subject of the application and related drugs, and reports in the scientific literature involving the drug that is the subject of the application. An adequate summary and bibliography of reports in the scientific literature will ordinarily suffice. (The applicant must identify at the time of each report submission each drug he considers related to the subject drug.)

(3) Experience, investigations, studies, or tests involving the chemical or physical properties or any other properties of the drug; such as, its behavior or properties in relation to microorganisms, including both the effects of the drug on microorganisms and the effects of microorganisms on the drug.

(4) The information required by this section shall include, when known, adequate identification of its source, including the name and post office address of the person who furnished such information.

(5) Copies of all mailing pieces and other labeling, and if it is a prescription drug all advertising, other than that contained in the application, used in promoting the drug; and copies of the currently used package labeling that gives full information for use of the drug, whether or not such labeling is contained in the application.

(6) Information concerning the quantity of the drug distributed, in a manner and form that facilitates estimates of the incidence of any adverse effects reported to be associated with the use of the drug. This does not require disclosure of financial or pricing data.

(7) Information concerning any previously unreported changes from the conditions described in an application, including changes conforming to the conditions of § 130.9(a)(5).

(b) The applicant shall submit to the Food and Drug Administration copies of the records and reports described in paragraph (a) of this section (except routine assay and control records) appropriately identified with the new-drug application(s) to which they relate, as follows. Such copies, including form FD-1639, shall be submitted in duplicate, except that other individual patient case reports may be submitted in single copy. Each report for human-use drugs that forwards an advertisement or promotional labeling pursuant to subparagraph (3) of this paragraph or a periodic report pursuant to subparagraph (4) of this paragraph shall be accompanied by a completed transmittal form FD 2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) or FD 2252 (Transmittal of Periodic Reports for Drugs for Human Use), respectively. Forms are obtainable from the Food and Drug Administration, Department of Health, Education, and Welfare, 200 C Street NW, Washington, D.C. 20204.

(1) Immediately upon receipt by the applicant, complete records or reports covering information of the following kinds:

(i) Information concerning any mixup in the drug or its labeling with another article.

(ii) Information concerning any bacteriological, or any significant chemical, physical, or other change or deterioration in the drug, or any failure of one or more distributed batches of the drug to meet the specifications established for it in the new-drug application.

(2) As soon as possible, and in any event within 15 working days of its receipt by the applicant, complete records and reports concerning any information of the following kinds:

(i) Information concerning any unexpected side effect, injury, toxicity, or sensitivity reaction or any unexpected incidence or severity thereof associated

with clinical uses, studies, investigations, or tests, whether or not determined to be attributable to the drug, except that this requirement shall not apply to the submission of information described in a written communication to the applicant from the Food and Drug Administration as types of information that may be submitted at other designated intervals. "Unexpected" as used in this subdivision refers to conditions or developments not previously submitted as part of the new-drug application or not encountered during clinical trials of the drug, or conditions or developments occurring at a rate higher than shown by information previously submitted as part of the new-drug application, or than encountered during such clinical trials.

(ii) Information concerning any unusual failure of the drug to exhibit its expected pharmacological activity.

(3) When mailing pieces, any other labeling, and advertising are devised for promotion of the drug, specimens shall be submitted at the time of initial dissemination of such labeling and at the time of initial publication of any advertisement for a prescription drug. Mailing pieces and labeling that are designed to contain samples of a drug shall be complete except for omission of the drug.

(4) All the kinds of information described in paragraph (a) of this section, other than that submitted under the provisions of subparagraphs (1), (2), and (3) of this paragraph, shall be submitted at the following intervals, unless otherwise ordered in a written communication from the Commissioner:

(i) If the drug is intended for administration to man, within intervals of 3 months beginning with the date of approval of the application during the first year following such date; within intervals of 6 months during the second year following such date; and at yearly intervals thereafter.

(ii) If the drug is intended solely for administration to animals, at intervals within 6 months beginning with the date of approval of the application during the first year following such date, and at yearly intervals thereafter: Provided, however, that such reports are not required from applicants to the extent that the reporting obligation is based on their manufacture of complete medicated feed.

(iii) Whenever an applicant is required to submit reports under the provisions of subdivision (i) or (ii) of this subparagraph with respect to more than one approved application for preparations containing the same drug so that the same item(s) of information is (are) required to be reported for more than one application, he may elect to submit as part of the report for one such application all the information common to such applications in lieu of reporting separately and repetitively on each. The applicant shall state when this is done and identify all the applications for which the reports are submitted.

(iv) The submitted copies of records and reports shall include all the required information that was received or otherwise obtained by the applicant during the designated intervals.

(5) On written order of the Commissioner, within the time stated in such order or agreed to by the applicant and the Commissioner, any designated records or reports containing the kinds of information described in this section.

(c) The reports submitted under the provisions of this section are not required to furnish the names and addresses of individual patients unless the applicant is notified in writing by the Food and Drug Administration that individual patient identification is required with respect to designated reports in order to permit further investigation or because there is reason to believe that such reports do not represent actual results obtained.

(d) The applicant shall upon request of any properly authorized officer or employee of the Department, at reasonable times, permit such officers to have access to and copy and verify any records and reports established and maintained under the provisions of this section.

(e) If the Food and Drug Administration finds that the applicant has failed to establish a system for maintaining required records, or has repeatedly or deliberately failed to maintain such records or to make required reports, in accordance with the provisions of this section, or that the applicant has refused to permit access to, or copying or verification of such records or reports, the Commissioner shall give the applicant due notice and opportunity for a hearing on the question of whether to withdraw the approval of the application, as provided in section 130.14 and 130.27.

(f) Upon written request of the applicant, stating reasonable grounds therefor, the Commissioner will make available any information in possession of the Food and Drug Administration of the kinds the applicant is required to maintain under the provisions of this section, except information readily available to the applicant from other sources or information which the Commissioner concludes must be considered confidential.

(g) The "applicant" required to establish and maintain records and make reports required by this section and under the regulations in section 130.35 includes any person whose name appears on the labeling of the drug as its manufacturer, packer, or distributor under an approval or who is engaged in the manufacturing, processing, packing, or labeling of the drug under an approval of the application or any supplement to it; Provided, however, that in order to avoid unnecessary duplication in the submission of reports any such applicant's obligation to submit a report may be met by its submission on his behalf, designated as such, by another person responsible for reporting.

Conditions of Approval of a New Drug Application

The signing of the new drug application form is regarded as a commitment on your part that:

> All representations in the application apply to the drug produced until an approved supplement to the application provides for a change or a change is made in conformance with other provisions of § 130.9 of the new-drug regulations.
>
> The labeling and advertising for the drug will prescribe, recommend, or suggest its use only under the conditions stated in the labeling which is part of this application; and if the article is a prescription drug, it is understood that any labeling which furnishes or purports to furnish information for use or which prescribes, recommends, or suggests a dosage for use of the drug will contain the same information for its use, including indications, effects, dosages, routes, methods, and frequency and duration of administration, any relevant warnings, hazards, contra-indications, side effects, and precautions, as that contained in the labeling which is part of this application in accord with § 1.106(b) (21 CFR 1.106(b)).

Section 505(e) of the Federal Food, Drug, and Cosmetic Act provides for approval of the application to be withdrawn if: clinical or other experience, tests, or other scientific data show that the drug is unsafe or not shown to be safe for use; further information indicates there is a lack of substantial evidence that the drug will have the effect it is represented to have; the application contains an untrue statement of material fact; the applicant fails to establish or maintain required records or make required reports; new information shows that the methods, facilities, or controls used in the manufacture, processing, and packing of the drug are inadequate to assure and preserve its identity, strength, quality, and purity; or the labeling of the drug is false and misleading.

The drug may not be labeled with another distributor's name, or repacked, or relabeled by another person unless provided for in the approved application or in conformance with § 130.9 of the new drug regulations.

Section 301(l) of the Act prohibits the use in the labeling, or in any advertising, of any representation or suggestion that an application with respect to the drug is approved under section 505, or that the drug complies with the provisions of that section.

The approval of this application under section 505 in no way relieves you of the responsibility for complying with all other provisions of the Act.

1-69

Exhibit 2

Exhibit 2

Suppl. #	Application Date(s)	Application (ETH.MESH.____)
S-001	10/30/1969	09629721–09629858
S-002	6/14/1971 10/28/1971 (amendment)	09630237–09630340 09630186–09630232 (amendment)
S-003	5/15/1972	09630724–09630739
S-004	11/10/1972	09630676–09630678
S-005	5/3/1973 (letter) 5/25/1973 (final labeling)	09630648 (letter agreeing to changes) 09630641–09630647 (final labeling)
S-006	10/29/1973	09630955–09630982
S-007	7/10/1974 (annual report)	09630991–09631140
S-008	12/19/1974	09631414–09631453
S-009	2/26/1975 (original) 5/22/1975 (1st amend.) 8/8/1975 (2nd amend.)	09631339–09631389 (original) 09631251–09631325 (1st amend.) 09631178–09631244 (2nd amend.)
S-010	3/25/1975	09631467– 09631500
S-011	7/15/1976 (annual report)	09631714–09631941
S-012	11/16/1977 (orig.) 9/19/1978 (1st amend.) 8/14/1979 (2nd amend.) 2/15/1980 (3rd amend.)	09632230–09632266 (orig.) 09632622–09632646 (1st amend.) 09632875–09632896 (2nd amend.) 09632870 (3rd amend.)
S-013	11/22/1977 (orig.) 9/19/1978 (amend.)	09632272–09632311 (orig.) 09632653–09632671 (amend.)
S-014	2/10/1978	09632321–09632328
S-015	6/30/1978	09632336–09632350
S-016	8/18/1978 (orig.) 1/5/1979 (amend.)	09632611–09632618 (orig.) 09632850–09632858 (amend.)
S-017	9/20/1978 (orig.) 5/22/1979 (amend.)	09632678–09632757 (orig.) 09632935–09632957 (amend.)
S-018	11/22/1978	09632777–09632847
S-019	7/9/1979	09632965–09632976
S-020	12/28/1979	09632987–09633000

Suppl. #	**Application Date(s)**	**Application (ETH.MESH.____)**
S-021	5/7/1980	09633015–09633023
S-1 [1980]	9/19/1980	09633031–09633062
S-2 [1980]	10/14/1980	09633216–09633241
S26	2/24/1983	09633366–09633381
S27	12/1/1983	09633429–09633436
S28	2/29/1984 (orig.) 9/13/1984 (amend.)	09633463–09633769 (orig.) 09633771–09633903 (amend.)
S29	11/22/1985	09634008–09634018
S30	3/14/1986	09634024–09634048
S31	10/24/1986	09634108–09634132
S33	7/31/1987	09634190–09634206
S34	9/8/1988	09634311–09634318
S35	2/16/1990	09634358–09634369

Exhibit 3

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
ROCKVILLE, MARYLAND 20852

RECEIVED
MAY 11 1970
P. V. BUDAY

NDA 16-374/S-001

MAY 8 1970

Ethicon, Incorporated
Attention: Dr. Paul V. Budsy
Somerville, New Jersey 08876

Gentlemen:

We acknowledge the receipt on November 3, 1969, of your supplemental new drug application dated October 30, 1969, submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prolene Polypropylene Suture (Nonabsorbable Surgical Suture, U.S.P., Type B).

The supplemental application provides for revision of the packaging procedures and packaging materials employed exclusively for the blue pigmented monofilament, sizes 00, 000, 4-0, and 5-0.

We have completed the review of this supplemental application and it is approved. Our letter of April 16, 1969, detailed the conditions relating to the approval of this application.

Yours truly,

Marvin Seife, M.D.
Director
Office of Marketed Drugs
Bureau of Drugs

Exhibit 4

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
ROCKVILLE, MARYLAND 20852

NDA 16-374/S-001

JUN 29 1970

RECEIVED

JUL 1 1970

P. V. BUDAY

Ethicon, Incorporated
Attention: Dr. Paul V. Buday
Somerville, New Jersey 08876

Gentlemen:

Reference is made to your supplemental new drug application of October 30, 1969, submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prolene Polypropylene Suture (Nonabsorbable Surgical Suture, U.S.P., Type B).

This communication is intended to amend the letter issued May 8, 1970, from this Administration, as discussed by telephone on June 24, 1970, between your representative, Mr. Robert J. Semple, and Dr. Nathan R. Rosenthal of this Office.

The supplemental application provides for revision of the packaging procedures and packaging materials employed for the suture sizes 7/0 thru 2, with and without needles, clear or pigmented, including those articles provided for in the letter issued May 8, 1970.

It is understood that the action of this letter only broadens the scope of the provision paragraph of our approved letter issued May 8, 1970.

Yours truly,

Marvin Seife

Marvin Seife, M.D.
Director
Office of Marketed Drugs
Bureau of Drugs

Exhibit 5

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
ROCKVILLE, MARYLAND 20852

NDA 16-374/S-002

AUG 17 1972

RECEIVED

AUG 21 1972

P. V. BUDAY

Ethicon, Incorporated
Attention: Dr. Paul V. Buday
Somerville, New Jersey 08876

Gentlemen:

We acknowledge the receipt on July 7, 1972 of your communication dated July 5, 1972 enclosing printed labeling pursuant to your supplemental new drug application dated June 14, 1971 for "Prolene Polypropylene Suture (Nonabsorbable Surgical Suture, U.S.P.)".

We have completed the review of this supplemental application as amended and it is approved. Our letter of April 16, 1969, detailed the conditions relating to the approval of this application.

Sincerely yours,

Frederick J. Grigsby, M.D.

Frederick J. Grigsby, M.D.
Deputy Director
Division of Surgical-Dental
Drug Products
Office of Scientific Evaluation
Bureau of Drugs

Exhibit 6

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
ROCKVILLE, MARYLAND 20852

NDA 16-374/S-003

AUG 1 1972

RECEIVED

AUG

Ethicon, Incorporated
Attention: Dr. Paul V. Buday
Somerville, New Jersey 08876

Gentlemen:

We acknowledge the receipt on May 22, 1972 of your supplemental new drug application dated May 15, 1972 submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prolene Polypropylene Suture (Nonabsorbable Surgical Suture, U.S.P.).

The supplemental application provides for the Chicopee Manufacturing Company, Lumite-Division, Cornelia, Georgia to be an alternate facility for the extrusion of monofilament from polypropylene pellets.

We have completed the review of this supplemental application and it is approved. Our letter of April 16, 1969 detailed the conditions relating to the approval of this application.

Sincerely yours,

Frederick J. Grigsby M.D.

Frederick J. Grigsby, M.D.
Deputy Director
Division of Surgical-Dental
Drug Products
Office of Scientific Evaluation
Bureau of Drugs

Exhibit 7

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
ROCKVILLE, MARYLAND 20852

NDA 16-374

APR 26 1973

Ethicon, Incorporated
Attention: Dr. Paul V. Buday
Somerville, New Jersey 08876

Gentlemen:

We acknowledge the receipt on January 26, 1973 of your communication dated January 25, 1973 pertaining to your new drug application for "Prolene Polypropylene Suture (Nonabsorbable Surgical Suture, U.S.P.)."

Your communication is submitted in response to our conference of November 29, 1972.

As you know, we have recently reviewed the package insert for Prolene and recommend the following change be made in the ADVERSE REACTIONS section in order to furnish adequate information for the safe use of the drug:

"Transitory local inflammatory reactions have been reported."

Please let us know promptly your proposal in regard to the above recommendation.

Sincerely yours,

Margaret F. Clark, M.D. for

George F. Leong, Ph.D.
Acting Director
Division of Surgical-Dental
Drug Products
Office of Scientific Evaluation
Bureau of Drugs

Exhibit 8

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
ROCKVILLE, MARYLAND 20852

NDA 16-374/S-005

JUN 26 1973

RECEIVED
JUN 28 1973
P. V. BUDAY

Ethicon, Incorporated
Attention: Dr. Paul V. Buday
Somerville, New Jersey 08876

Gentlemen:

We acknowledge the receipt on May 29, 1973 of your supplemental new drug application dated May 25, 1973 submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prolene Polypropylene Suture (Nonabsorbable Surgical Suture, U.S.P.).

The supplemental application provides for final printed labeling containing revised wording of the Adverse Reactions section as requested in our letter of April 26, 1973.

We have completed the review of this supplemental application and it is approved. Our letter of April 16, 1969 detailed the conditions relating to the approval of this application.

Sincerely yours,

Margaret Clark, M.D.

Margaret A. Clark, M.D.
Acting Director
Division of Surgical-Dental
Drug Products
Office of Scientific Evaluation
Bureau of Drugs

Exhibit 9

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
ROCKVILLE, MARYLAND 20852

NDA 16-374/S-004

SEP 10 1973

Ethicon, Incorporated
Attention: Dr. Paul V. Buday
Somerville, New Jersey 08876

Gentlemen:

We acknowledge the receipt on August 15, 1973 of your communication dated August 14, 1973 regarding your supplemental new drug application of November 10, 1972 submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prolene Polypropylene Suture (Nonabsorbable Surgical Suture, U.S.P.).

The supplemental application provides for reinstating molecular weight determination by intrinsic viscosity measurement as a raw material specification for both pigmented and unpigmented pelletized polypropylene resin (Novamont), and for changing the acceptable melt index range for pigmented pelletized polypropylene resin (Novamont) from 3-5 to 4-7. The raw material specification for melt index for unpigmented pelletized polypropylene resin will remain as a range of 3-5.

We have completed the review of this supplemental application as amended and it is approved. Our letter of April 16, 1969 detailed the conditions relating to the approval of this application.

Sincerely yours,

Margaret Clark, M.D.

Margaret A. Clark, M.D.
Acting Director
Division of Surgical-Dental
Drug Products
Office of Scientific Evaluation
Bureau of Drugs

Exhibit 10

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
ROCKVILLE, MARYLAND 20852

RECEIVED
MAR 6 1974
P. V. BUDAY

NDA 16-374/S-006

MAR 0 1 1974

Ethicon, Incorporated
Attention: Dr. Paul V. Buday
Somerville, New Jersey 08876

Gentlemen:

Reference is made to your supplemental new drug application of October 29, 1973, submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prolene Polypropylene Suture (Nonabsorbable Surgical Suture, U.S.P.).

The supplemental application provides for the manufacture, processing, packaging, labeling, and sterilization of this drug in Ethicon's facility located at U.S. 67, San Angelo, Texas 76901.

The approval of this supplemental application is based upon the proper installation and validation before production of the sterilization chamber and gas chromatographic equipment.

We have completed the review of this supplemental application, and it is approved. Our letter of April 16, 1969, detailed the conditions relating to the approval of this application.

Sincerely yours,

Margaret A. Clark, M.D.

Margaret A. Clark, M.D.
Acting Director
Division of Surgical-Dental
Drug Products
Office of Scientific Evaluation
Bureau of Drugs

Exhibit 11

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
ROCKVILLE, MARYLAND 20852

RECEIVED

NDA 16-374/S-007

NOV 19 1974

P. V. BUDAY

Ethicon, Incorporated
Attention: Dr. Paul V. Buday
Somerville, New Jersey 08876

NOV 18 1974

Gentlemen:

We acknowledge the receipt on July 15, 1974, of your communication dated July 10, 1974, reporting experience, as required by the provisions of Title 21 CFR 310.300 and section 505(j) of the Federal Food, Drug, and Cosmetic Act for the preparation Prolene Polypropylene Suture (nonabsorbable surgical suture, U.S.P.).

The report contains information regarding the replacement of the Kodacel/Surlyn 2.5 mil laminate as the top component of the overwrap or secondary protective package, with a polypropylene/Surlyn 2.0 mil laminate as supplied by the American Can Company (PZ-5516.51). A change of this nature falls under the provisions of 21 CFR 314.8(a)(2) and necessitates the submission and prior approval of a supplemental application.

It is understood from the discussion by telephone on October 15, 1974, between your representative Mr. Robert Semple and Mr. Stanley Koch of this Administration that the sterility stability studies using the polypropylene/Surlyn 1601 overwrap, as reported in your July 10, 1974, periodic report, will be continued for a period of not less than 5 years, data submitted as available, and lots found to fall outside approved specifications for the drug, including product sterility, will be removed from the market.

We have completed the review of this supplemental application and it is approved. Our letter of April 16, 1969, detailed the conditions relating to the approval of this application.

Please submit two market packages of the drug, when available, incorporating the changes provided for by this supplemental application.

Sincerely yours,

Margaret A. Clark, M.D.

Margaret A. Clark, M.D.
Acting Director
Division of Surgical-Dental
Drug Products
Office of Scientific Evaluation
Bureau of Drugs

Exhibit 12

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
ROCKVILLE, MARYLAND 20852

NDA 16-374/S-008

RECEIVED

JAN 17 1975

P. V. BUDAY

JAN 16 1975

Ethicon, Inc.
Attention: Dr. Paul V. Buday
Somerville, New Jersey 08876

Gentlemen:

Reference is made to your supplemental new drug application of December 19, 1974, submitted pursuant to section 505(b) of the Federal, Food, Drug, and Cosmetic Act for Prolene Polypropylene Suture (nonabsorbable surgical suture, U.S.P.).

The supplemental application provides for the marketing of monofilament Prolene sutures in blue pigmented suture sizes 8/0, 9/0, and 10/0.

We have completed the review of this supplemental application and it is approved. Our letter of April 16, 1969, detailed the conditions relating to the approval of this application.

Please submit one market package of a representative product of each size of pigmented monofilament Prolene polypropylene sutures provided for by this supplemental application.

Yours sincerely,

Margaret A. Clark, M.D.

Margaret A. Clark, M.D.
Acting Director
Division of Surgical-Dental
Drug Products
Bureau of Drugs

Exhibit 13

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
ROCKVILLE, MARYLAND 20852

RECEIVED
JUN 5 1975
P. V. BUDAY

NDA 16-374/S-010

JUN 4 1975

Ethicon, Incorporated
Attention: Paul V. Buday, Ph.D.
Somerville, New Jersey 08876

Gentlemen:

Reference is made to your ~~supplemental new drug application of March~~ 25, 1975 submitted pursuant to section 505(b) of the Federal, Food, Drug, and Cosmetic Act for Prolene Polypropylene Suture (nonabsorbable surgical suture, U.S.P.)

The supplemental application provides for a "see-through" package for blue pigmented Prolene sutures, 8/0, 9/0, and 10/0 sizes, consisting of two overwraps, each envelope of which corresponds to the currently approved (S-007) polypropylene/Surlyn top laminate and paper/polyethylene/foil bottom component overwrap.

It is understood from the discussion by telephone on May 29, 1975 between your representative Dr. Paul V. Buday and Mr. Stanley Koch of this Administration that the stability studies to be performed on this new drug package, as described on p. 15 of your March 25, 1975 submission, will be conducted on two production lots of size 8/0, and two production lots of size 10/0, Prolene sutures at 25°C and at 37°C.

We have completed the review of this supplemental application and it is approved. Our letter of April 16, 1969 detailed the conditions relating to the approval of this application.

Please submit two market packages of the drug, when available, incorporating the changes provided for by this supplemental application.

Sincerely yours,
Clarence C. Gilkes, D.D.S.
for
Margaret A. Clark, M.D.
Acting Director
Division of Surgical-Dental
Drug Products
Bureau of Drugs

Exhibit 14

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
ROCKVILLE, MARYLAND 20852

SEP 22 1975

RECEIVED
SEP 23 1975
P. V. BUDAY

NDA 16-374/S-009

Ethicon Inc.
Attention: Paul V. Buday, Ph.D.
Route 22
Somerville, New Jersey 08876

Gentlemen:

CF PL SUBM. DATE)

Reference is made to your Supplemental New Drug Application of August 8, 1975, submitted pursuant to Section 505(b) of the Federal, Food, Drug, and Cosmetic Act for Prolene (Polypropylene) Suture, enclosing final printed labeling.

The supplemental application provides for revisions of suture size, needling, and labeling.

We have completed the review of this supplemental application and it is approved. Our letter of April 16, 1969, detailed the conditions relating to the approval of this application.

In addition, please note that the product may not be legally marketed until the Color Additive Regulation is amended to allow usage as provided for in Supplement S-009 and the present restriction under 21 CFR 8.4026(c) is removed.

Sincerely yours,

Margaret Clark, M.D.

Margaret A. Clark, M.D.
Acting Director
Division of Surgical-Dental
Drug Products
Bureau of Drugs

Exhibit 15

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
ROCKVILLE, MARYLAND 20852

NDA 16-374/S-011

RECEIVED
OCT 26 1976
P. V. BUDAY

OCT 22 1976

Ethicon, Inc.
Attention: Paul V. Buday, Ph.D.
Somerville, New Jersey 08876

Gentlemen:

We acknowledge the receipt on July 19, 1976, of your communication dated July 15, 1976, reporting experience, as required by the provisions of Title 21 CFR 310.300 and section 505(j) of the Federal Food, Drug, and Cosmetic Act for the preparation Prolene Polypropylene Suture (nonabsorbable surgical suture, U.S.P.).

The report contains information regarding the replacement of the 0.5 mil polypropylene/1.5 mil Surlyn film laminate as the top component of the outerwrap or secondary protective package, with a 0.5 mil polypropylene/2.0 mil Surlyn film as supplied by the American Can Company. A change of this nature falls under the provisions of 21 CFR 314.8(a)(2) and necessitates the submission and prior approval of a supplemental application.

We have completed the review of this supplemental application and it is approved. Our letter of April 16, 1969 detailed the conditions relating to the approval of this application.

Please submit two market packages of the drug, when available, incorporating the changes provided by this supplemental application.

Sincerely yours,

Clarence C. Gilkes, D.D.S.
for
Margaret A. Clark, M.D.
Director
Division of Surgical-Dental
Drug Products
Bureau of Drugs

Exhibit 16

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
ROCKVILLE, MARYLAND 20857

NDA 16-374/S014

MAY 12 1978

Ethicon, Inc.
Attention: Joan C. Kurjian
Somerville, NJ 08876

Gentlemen:

Please refer to your supplemental new drug application of February 10, 1978, submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prolene Polypropylene Suture (nonabsorbable surgical suture, U.S.P.).

The supplemental application provides for revised labeling for Prolene sutures with mechanically attached control release removable needles.

We have completed the review of this supplemental application and it is approved. Our letter of April 16, 1969, detailed the conditions relating to the approval of this application.

Sincerely yours,

Philip G. Walters, M.D.
Acting Director
Division of Surgical-Dental
Drug Products
Bureau of Drugs

Exhibit 17

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
ROCKVILLE, MARYLAND 20857

NDA 16-374/S-015

Ethicon, Inc.
Attention: Joan C. Kurjian
Somerville, NJ 08876

DEC 20 1978

Gentlemen:

We acknowledge the receipt on October 13, 1978, of your communication dated October 12, 1978, enclosing printed labeling pursuant to your supplemental new drug application dated June 30, 1978, for Prolene Polypropylene Suture (nonabsorbable surgical suture, U.S.P.).

The supplemental application provides for revised labels.

We have completed the review of this supplemental application and it is approved. Our letter of April 16, 1969, detailed the conditions relating to the approval of this application.

Sincerely yours,

Joseph K. Inscoe, Ph.D.
Acting Director
Division of SurgicalDental
Drug Products
Bureau of Drugs

Exhibit 18

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
ROCKVILLE, MARYLAND 20857

NDA 16-374/S-016

RECEIVED
APR 16 1979
J. C. KURJIAN

Ethicon, Inc.
Attention: Ms. J. C. Kurjian
Somerville, NJ 18876

Gentlemen:

We acknowledge the receipt on January 8, 1979, of your communication dated January 5, 1979, enclosing printed labeling pursuant to your supplemental new drug application dated August 18, 1978, for Prolene Polypropylene Suture Nonabsorbable Surgical Suture, USP.

The supplemental application provides for labeling revision.

We have completed the review of this supplemental application and it is approved. Our letter of April 16, 1969, detailed the conditions relating to the approval of this application.

Sincerely yours,

James P. Mann

James P. Mann, M.D.
Acting Director
Division of Surgical-Dental
Drug Products
Bureau of Drugs

Exhibit 19

DEPARTMENT OF HEALTH, EDUCATION AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
ROCKVILLE, MARYLAND 20857

NDA 16-374/S-018

Ethicon, Inc.
Attention: Ms. J. C. Kurjian
Somerville, New Jersey 08876

MAY 13 1979

Gentlemen:

Please refer to your supplemental new drug application of November 22, 1978, submitted pursuant to section 505(b) of the Federal Food, Drug and Cosmetic Act for Prolene Polypropylene Suture, Nonabsorbable Surgical Suture, U.S.P.

The supplemental application provides for the addition of a polyethylene suture retainer (needle park) to the currently approved packaging of Prolene suture products.

We have completed the review of this supplemental application and it is approved. Our letter of December 20, 1978, detailed the conditions relating to the approval of this application.

Sincerely yours,

James P. Mann

James P. Mann, M.D.
Acting Director
Division of Surgical-Dental
Drug Products
Bureau of Drugs

Exhibit 20

FOOD AND DRUG ADMINISTRATION
ROCKVILLE, MARYLAND 20857

NDA 16-374/S-019

RECEIVED
DEC 13 1979
J. C. KURJIAN

DEC 06 1979

Ethicon, Inc.
Attention: Ms. Joan C. Kurjian
Sommerville, NJ 08876

Dear Ms. Kurjian:

Please refer to your supplemental new drug application of July 9, 1979 submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prolene*Polypropylene Suture Clear and Pigmented Nonabsorbable Surgical Suture, U.S.P.

The supplemental application provides for a revised package insert.

We have completed the review of this supplemental application and it is approved. Our letter of April 10, 1969 detailed the conditions relating to the approval of this application.

Sincerely yours,

James P. Mann

James P. Mann, M.D.
Director
Division of Surgical-Dental
Drug Products
Bureau of Drugs

Exhibit 21

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
ROCKVILLE, MARYLAND 20857

NDA 16-374/S-017

RECEIVED

JAN 7 1980

J. C. KURJIAN

JAN 04 1980

Ethicon, Inc.
Attention: Ms. Joan C. Kurjian
Somerville, NJ 08876

Gentlemen:

Please refer to your resubmitted supplemental new drug application of May 22, 1979, submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prolene Polypropylene Suture Nonabsorbable Surgical Suture, USP.

The supplemental application as amended provides for the use of alternate secondary overwrap package components.

We have completed the review of this supplemental application and it is approved. Our letter of April 16, 1969, detailed the conditions relating to the approval of this application.

Sincerely yours,

James P. Mann

James P. Mann, M.D.
Director
Division of Surgical-Dental
Drug Products
Bureau of Drugs

Exhibit 22

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
ROCKVILLE, MARYLAND 20857

NDA 16-374/S-012

Ethicon, Inc.
Attention: Joan C. Kurjian
Somerville, New Jersey 08876

Gentlemen:

Please refer to your resubmitted new drug application of February 15, 1980 submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prolene ™ (Polypropylene Suture Nonabsorbable Surgical Suture, USP).

The supplemental application provides for the use of Sharpoint, Inc., of Mohton, Pennsylvania, as a partial processor of Prolene polypropylene suture.

We have completed the review of this supplemental application and it is approved. Our letter of April 10, 1969 detailed the conditions relating to the approval of this application.

Sincerely yours,

James P. Mann

James P. Mann, M.D.
Director
Division of Surgical-Dental
Drug Products
Bureau of Drugs

Exhibit 23

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
ROCKVILLE, MARYLAND 20857

NDA 16-374/S-013

Ethicon, Inc.
Attention: Joan C. Kurjian
Somerville, New Jersey 08876

APR 23 1980

Gentlemen:

Please refer to your resubmitted new drug application of February 15, 1980 submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prolene ™ (Polypropylene Suture Nonabsorbable Surgical Suture, USP).

The supplemental application provides for the use of Spingler and Tritt of Jestetten, West Germany, as a partial processor of Prolene polypropylene suture.

We have completed the review of this supplemental application and it is approved. Our letter of April 10, 1969 detailed the conditions relating to the approval of this application.

Sincerely yours,

James P. Mann, M.D.
Director
Division of Surgical-Dental
Drug Products
Bureau of Drugs

Exhibit 24

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
ROCKVILLE, MARYLAND 20857

RECEIVED
MAY 7 1980
HOWARD L. SCHRAYER

MAY 02 1980

NDA 11-397, 12-815, 16-374
17-804, 17-809, 17-472
17-482, 18-175, 18-176

Ethicon, Inc.
Attention: Ms. Joan C. Kurjian
Somerville, New Jersey 08876

Gentlemen:

Reference is made to your supplemental new drug application submitted pursuant to section 505(b) of the Federal Food, Drug and Cosmetic Act for the following products:

NDA 11-397 (S012) Silk Suture Nonabsorbable Surgical Suture, U.S.P.
NDA 12-815 (S010) Mersilene Polyester Suture Nonabsorbable Surgical Suture, U.S.P. (Dyed and Undyed).
NDA 16-374 (S020) Prolene Polypropylene Suture Nonabsorbable Surgical Suture, U.S.P. (Clear and Pigmented)
NDA 17-472 (S026) Vicryl (polyglactin 910) Suture Synthetic Absorbable Suture, Dyed.
NDA 17-482 (S021) Vicryl (polyglactin 910) Suture Synthetic Absorbable Suture, Undyed
NDA 17-804 (S020) Ethibond Polyester Suture Nonabsorbable Surgical Suture, U.S.P., Dyed
NDA 17-809 (S013) Ethibond Polyester Suture Nonabsorbable Surgical Suture, Undyed.
NDA 18-175 (S001) Coated Vicryl (Polyglactin 910) Suture Synthetic Absorbable Suture, Dyed.
NDA 18-176 (S001) Coated Vicryl (Polyglactin 910) Suture Synthetic Absorbable Suture, Undyed.

The supplemental applications provide for the use of the Cornelia, Georgia, facility as a raw material testing site.

We have completed the review of these supplemental applications and they are approved. Our previous letters detailed the conditions relating to the approval of the original applications.

Sincerely yours,

James P. Mann, M.D.
Director
Division of Surgical-Dental
Drug Products
Bureau of Drugs

Exhibit 25

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
SILVER SPRING, MARYLAND 20910

DEC 17 1980

Mr. Howard L. Schrayer
Director, Regulatory Affairs
Ethicon, Inc.
Research and Development Division
Somerville, New Jersey 08876

Ref: NDA 16-374

Dear Mr. Schrayer:

We have completed our review of your September 19, 1980 supplement to NDA 16-374 which requests approval for the use of alternate packaging material, i.e., coated Tyvek, for PROLENE polypropylene nonabsorbable sutures. Your supplement is approved.

Sincerely,

Robert G. Britain

for Victor Zafra
Acting Director
Bureau of Medical Devices

Exhibit 26

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
SILVER SPRING, MARYLAND 20910

JAN 6 1981

Mr. Howard L. Schrayer
Director, Regulatory Affairs
Ethicon, Inc.
Somerville, New Jersey 08876

Ref: NDA's 8-536, 16-374, 10-389,
17-472, 11-397, 17-482,
12-815, 17-804

Dear Mr. Schrayer:

The Food and Drug Administration (FDA) has completed its review of the following supplemental applications, dated May 7, 1980, to replace the present control release needle/suture attachment requirement with the specifications and procedure for testing described in the current USP for removable needles.

NDA 8-536
Catgut Suture (Plain and Chromic)
Absorbable Surgical Suture, USP, S-008

NDA 10-389
Catgut Suture (Plain and Chromic)
Absorbable Surgical Suture, USP, S-010

NDA 11-397
Silk Suture
Nonabsorbable Surgical Suture, USP,
(Dyed and White Virgin), S-013

NDA 12-815
Mersilene* Polyester Suture,
Nonabsorbable Surgical Suture, USP
(Dyed and Undyed), S-011

NDA 16-374
Prolene* Polypropylene Suture,
Nonabsorbable Surgical Suture, USP
(Clear and Pigmented), S-021

NDA 17-472
Vicryl* (Polyglactin 910) Suture,
Synthetic Absorbable Suture, USP
(Dyed), S-028

NDA 17-482
Vicryl (Polyglactin 910) Suture,
Synthetic Absorbable Suture,
(Undyed), S-023

NDA 17-804
Ethibond* Polyester Suture Nonabsorbable
Surgical Suture, USP
(Dyed), S-023

Your supplements have been approved.

Sincerely,

Victor Zafra
Acting Director
Bureau of Medical Devices

Exhibit 27

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
8757 Georgia Avenue
Silver Spring MD 20910

JAN 14 1981

RECEIVED

JAN 23 1981

HOWARD L. SCHRAYER

Mr. Howard L. Schrayer
Director, Regulatory Affairs
Ethicon, Inc.
Somerville, New Jersey 08876

Ref: NDA 16-374/S-2
PROLENE Polypropylene Suture

Dear Mr. Schrayer:

The Food and Drug Administration has completed its review of your supplemental application, dated October 14, 1980, which requests approval to market the PROLENE Polypropylene Suture, size 11-0. Your supplement is approved.

If you have any questions, please contact Carl A. Larson, Ph.D. at (301) 427-7156.

Sincerely,

Victor Zafra
Acting Director
Bureau of Medical Devices

Exhibit 28

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
8757 Georgia Avenue
Silver Spring MD 20910

RECEIVED

APR 1 1 1983

R. H. O'HOLLA

APR 7 1983

Mr. Robert H. O'Holla
Department Manager
Regulatory Affairs
Research and Development Division
Ethicon, Inc.
Route 22
Somerville, New Jersey 08876

Re: N16374/S26
PROLENE* Polypropylene Suture
Nonabsorbable Surgical Suture,
USP (Clear and Pigmented)
Filed: March 4, 1983

Dear Mr. O'Holla:

The Food and Drug Administration (FDA) has completed its evaluation of your premarket approval application (PMA) supplement which requested approval for the use of polyethylene as an alternate material to be used as a thermoformed suture organizer. Based upon the information submitted, the PMA supplement is approved subject to the conditions described in the "Conditions of Approval for a PMA Supplement" (enclosed).

You may begin production and marketing of the device as modified by your PMA supplement upon receipt of this letter.

If you have any questions concerning the approval of this supplemental application, please contact Carl A. Larson, Ph.D., at (301) 427-7156.

Sincerely yours,

Robert G Britain

Robert G. Britain
Associate Director for
Device Evaluation
Office of Medical Devices
National Center for Devices
and Radiological Health

Enclosure

*Trademark

Revised: March 10, 1983

CONDITIONS OF APPROVAL FOR A PMA SUPPLEMENT

Adverse Reaction and Device Defect Reporting.

You shall submit a written report to the Food and Drug Administration (FDA), National Center for Devices and Radiological Health, Office of Medical Devices, Document Control Center (HFK-20), 8757 Georgia Avenue, Silver Spring, Maryland 20910 within 10 days after you receive or have knowledge of information about:

(1) a mixup of the device or its labeling with another article;

(2) any significant chemical, physical, or other change or deterioration in the device, or any failure of one or more of the devices to meet the specifications established in the application;

(3) any adverse reaction, side effect, injury, toxicity, or sensitivity reaction that is attributable to the device and has not been addressed by the device's labeling; and

(4) any adverse reaction, side effect, injury, toxicity, or sensitivity reaction that is attributable to the device and has been addressed by the device's labeling, but is occurring with unexpected severity or frequency.

Note: All conditions of approval are subject to change upon publication of a final premarket approval regulation.

Exhibit 29

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

RECEIVED

MAR 15 1984

R. H. O'HOLLA

Food and Drug Administration
8757 Georgia Avenue
Silver Spring MD 20910

MAR 18 1984

Mr. Robert H. O'Holla
Department Manager
Regulatory Affairs
Research and Development Division
Ethicon, Inc.
Route 22
Somerville, New Jersey 08876

Re: N16-374/S27
PROLENE™ Polypropylene Suture
Nonabsorbable Surgical Suture,
USP (Clear and Pigmented)
Filed: December 9, 1983

Dear Mr. O'Holla:

The Food and Drug Administration (FDA) has completed its evaluation of your premarket approval application (PMA) supplement which requested approval for the use of polypropylene as an alternate material to be used as a thermoformed suture organizer. Based upon the information submitted, the PMA supplement is approved subject to the conditions described in the "Conditions of Approval for a PMA Supplement" (enclosed).

You may begin production and marketing of the device as modified by your PMA supplement upon receipt of this letter.

If you have any questions concerning the approval of this supplemental application, please contact Thomas J. Callahan, Ph.D., at (301) 427-7238.

Sincerely yours,

Robert G. Britain

Robert G. Britain
Acting Director
Office of Device Evaluation
National Center for Devices
and Radiological Health

Enclosure

I

Revised: January 10, 1984

CONDITIONS OF APPROVAL FOR A PMA SUPPLEMENT

Adverse Reaction and Device Defect Reporting.

You shall submit a written report to the Food and Drug Administration (FDA), National Center for Devices and Radiological Health, Document Mail Center (HFZ-401), 8757 Georgia Avenue, Silver Spring, Maryland 20910 within 10 days after you receive or have knowledge of information about:

(1) a mixup of the device or its labeling with another article;

(2) any significant chemical, physical, or other change or deterioration in the device, or any failure of one or more of the devices to meet the specifications established in the application;

(3) any adverse reaction, side effect, injury, toxicity, or sensitivity reaction that is attributable to the device and has not been addressed by the device's labeling; and

(4) any adverse reaction, side effect, injury, toxicity, or sensitivity reaction that is attributable to the device and has been addressed by the device's labeling, but is occurring with unexpected severity or frequency.

Note: All conditions of approval are subject to change upon publication of a final premarket approval regulation.

Exhibit 30

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
8757 Georgia Avenue
Silver Spring MD 20910

JUN 10 1985

Mr. Robert H. O'Holla
Department Manager
Regulatory Affairs
Research and Development Division
Ethicon, Inc.
Route 22
Somerville, New Jersey 08876

Re: N16-374/S28
PROLENE™ Polypropylene Suture
Nonabsorbable Surgical
Suture, USP (Clear and
Pigmented)
Filed: March 5, 1984
Amended: September 18, 1984; and
May 20, 1985

Dear Mr. O'Holla:

The Center for Devices and Radiological Health of the Food and Drug Administration has reviewed your premarket approval application (PMA) supplement, which requested approval for an alternate source of polypropylene resin raw material. Based upon the information submitted, the PMA supplement is approved subject to the conditions described in the "Conditions of Approval" (enclosed).

You may begin production and marketing of the device as modified by your PMA supplement upon receipt of this letter.

If you have any questions concerning the approval of this supplemental application, please contact Thomas Callahan, Ph.D., at (301) 427-7238.

Sincerely yours,

Carl A. Larson

Carl A. Larson, Ph.D.
Director
Division of Surgical
and Rehabilitation Devices
Center for Devices
and Radiological Health

Enclosure

RECEIVED

JUN 12 1985

R. H. O'HOLLA

MAY 1 1985

I

CONDITIONS OF APPROVAL

Approved Labeling. As soon as possible, and before commercial distribution of your device, submit two copies of an amendment to this PMA submission with copies of all approved labeling in final printed form to the Food and Drug Administration (FDA), Center for Devices and Radiological Health, PMA Document Mail Center (HFZ-401), 8757 Georgia Avenue, Silver Spring, Maryland 20910.

Premarket Approval Application (PMA) Supplement. Before making any change that could affect the safety or effectiveness of the device, submit a PMA supplement for review and approval by Center for Devices and Radiological Health (CDRH). Such changes may include, but are not limited to:

(1) new indications for use;

(2) labeling changes;

(3) changes in existing manufacturing facilities, methods or quality control procedures;

(4) the use of a different facility or establishment to manufacture, process, or package the device;

(5) changes in sterilization procedures;

(6) changes in packaging;

(7) changes in the performance or design specification, circuits, parts, components, accessories, ingredients, or physical layout of the device; and

(8) extension of the expiration date of the device based on data obtained under a new or revised testing protocol that has not been approved by CDRH. If the protocol has been approved, the change shall be submitted along with the supporting data in the next periodic report required in the PMA approval order. An approved protocol is one included in FDA guidelines applicable to the device or in a PMA submission for the device for which the approval order granted the expiration dating requested by you. Otherwise, you must submit and obtain CDRH approval of a PMA supplement for an expiration dating protocol.

Changes described below that enhance the safety of the device or safety in the use of the device may be placed into effect before your receipt of a written FDA order approving the PMA supplement provided that:

(1) the PMA supplement and its mailing cover are plainly marked "Special PMA Supplement - Changes Being Effected";

(2) the PMA supplement provides a full explanation of the basis for the changes;

(3) the applicant has received acknowledgement of FDA receipt of the PMA supplement;

(4) the PMA supplement specifically identifies the date that such changes are being effected; and

(5) the changes are among the following:

(a) labeling changes that add or strengthen a contraindication, warning, precaution, or adverse reaction or effect;

(b) labeling changes that add or strengthen an instruction that is intended to enhance the safe use of the device;

(c) labeling changes that delete misleading, false, or unsupported indications; or

(d) changes in the manufacturing process or quality controls that add a new specification or test method, or otherwise provide additional assurance of purity, identity, strength or reliability of the device.

You need submit only three (3) copies of a PMA supplement and include only information relevant to the proposed or effected changes in the device. The submission shall include a separate section that identifies all changes for which approval is being requested. You shall submit additional copies and additional information if requested by CDRH.

FDA may, as experience permits, issue guidelines listing specific types of changes that do not require FDA approval before implementation.

Post-Approval Reports. Continued approval of your device is contingent upon the submission of 2 copies of post-approval reports to the Food and Drug Administration, Center for Devices and Radiological Health, PMA Document Mail Center (HFZ-401), 8757 Georgia Avenue, Silver Spring, Maryland 20910 at intervals of 1 year from the date of this letter. The required contents of these reports will be described in the final order for the premarket approval procedural regulation which will be published in the FEDERAL REGISTER in the future. Until this regulation is published in final form, each periodic report shall consist of information that previously has not been submitted as part of a PMA supplement and which you have obtained since the last post-approval report or since receipt of this letter, whichever is later:

(1) a bibliography and summary of reports in the scientific literature involving the device and unpublished reports of in vitro, animal and clinical experience studies, investigations, and tests conducted by, reported to, or reasonably available to you involving the device or a related device--if, after reviewing the bibliography and summary, CDRH concludes that it needs a copy of the published and unpublished reports, CDRH will notify you that copies of such reports shall be submitted;

(2) written promotional material; and

(3) a description of changes made in the device not previously submitted in a PMA supplement.

Adverse Reaction and Device Defect Reporting. You shall submit 3 copies of a written report to the Food and Drug Administraiton, Center for Devices and Radiological Health (CDRH), 8757 Georgia Avenue, Silver Spring, Maryland 20910 within 10 days after you receive or have knowledge of information about:

(1) a mixup of the device or its labeling with another article;

Exhibit 31

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
8757 Georgia Avenue
Silver Spring MD 20910

RECEIVED
JAN 27 1986
R. H. O'HOLLA

JAN 2 3 1986

Mr. Robert H. O'Holla
Director
Regulatory Affairs
Research and Development Division
Ethicon, Inc.
Somerville, New Jersey 08876

Re: N16-374/S29
PROLENE™ Polypropylene
Nonabsorbable Surgical
Suture, USP
Filed: November 29, 1985

Dear Mr. O'Holla:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its evaluation of your premarket approval application (PMA) supplement, which requested approval for the addition of a thermoformed primary suture package as an alternate to the currently approved package. Based on data previously reviewed for this packaging material for similar products and on the information submitted, the PMA supplement is approved subject to the conditions described in the "Conditions of Approval" (enclosed).

You may begin production and marketing of the device as modified by your PMA supplement upon receipt of this letter.

If you have any questions concerning the approval of this supplemental application, please contact Kenneth A. Palmer, Ph.D., at (301) 427-7238.

Sincerely yours,

Carl A. Larson

Carl A. Larson, Ph.D.
Director, Division of Surgical
and Rehabilitation Devices
Office of Device Evaluation
Center for Devices
and Radiological Health

CONDITIONS OF APPROVAL

Approved Labeling. As soon as possible, and before commercial distribution of your device, submit two copies of an amendment to this PMA submission with copies of all approved labeling in final printed form to the Food and Drug Administration (FDA), Center for Devices and Radiological Health, PMA Document Mail Center (HFZ-401), 8757 Georgia Avenue, Silver Spring, Maryland 20910.

Advertisement. No advertisement for this device shall recommend or imply that the device may be used for any use that is not mentioned in the approved labeling for the device. All written promotional material shall include a brief statement of the intended uses of the device and relevent warnings, precautions, side effects, and contraindictions.

Premarket Approval Application (PMA) Supplement. Before making any change that could affect the safety or effectiveness of the device, submit a PMA supplement for review and approval by Center for Devices and Radiological Health (CDRH). Such changes may include, but are not limited to:

(1) new indications for use;

(2) labeling changes;

(3) changes in existing manufacturing facilities, methods or quality control procedures;

(4) the use of a different facility or establishment to manufacture, process, or package the device;

(5) changes in sterilization procedures;

(6) changes in packaging;

(7) changes in the performance or design specification, circuits, parts, components, accessories, ingredients, or physical layout of the device; and

(8) extension of the expiration date of the device based on data obtained under a new or revised testing protocol that has not been approved by CDRH. If the protocol has been approved, the change shall be submitted along with the supporting data in the next periodic report required in the PMA approval order. An approved protocol is one included in FDA guidelines applicable to the device or in a PMA submission for the device for which the approval order granted the expiration dating requested by you. Otherwise, you must submit and obtain CDRH approval of a PMA supplement for an expiration dating protocol.

Changes described below that enhance the safety of the device or safety in the use of the device may be placed into effect before your receipt of a written FDA order approving the PMA supplement provided that:

(1) the PMA supplement and its mailing cover are plainly marked "Special PMA Supplement - Changes Being Effected";

(2) the PMA supplement provides a full explanation of the basis for the changes;

(3) the applicant has received acknowledgement of FDA receipt of the PMA supplement;

(4) the PMA supplement specifically identifies the date that such changes are being effected; and

(5) the changes are among the following:

(a) labeling changes that add or strengthen a contraindication, warning, precaution, or adverse reaction or effect;

(b) labeling changes that add or strengthen an instruction that is intended to enhance the safe use of the device;

(c) labeling changes that delete misleading, false, or unsupported indications; or

(d) changes in the manufacturing process or quality controls that add a new specification or test method, or otherwise provide additional assurance of purity, identity, strength or reliability of the device.

You need submit only three (3) copies of a PMA supplement and include only information relevant to the proposed or effected changes in the device. The submission shall include a separate section that identifies all changes for which approval is being requested. You shall submit additional copies and additional information if requested by CDRH.

FDA may, as experience permits, issue guidelines listing specific types of changes that do not require FDA approval before implementation.

Post-Approval Reports. Continued approval of your device is contingent upon the submission of 2 copies of post-approval reports to the Food and Drug Administration, Center for Devices and Radiological Health, PMA Document Mail Center (HFZ-401), 8757 Georgia Avenue, Silver Spring, Maryland 20910 at intervals of 1 year from the date of this letter. The required contents of these reports will be described in the final order for the premarket approval procedural regulation which will be published in the FEDERAL REGISTER in the future. Until this regulation is published in final form, each periodic report shall consist of information that previously has not been submitted as part of a PMA supplement and which you have obtained since the last post-approval report or since receipt of this letter, whichever is later;

(1) a bibliography and summary of reports in the scientific literature involving the device and unpublished reports of in vitro, animal and clinical experience studies, investigations, and tests conducted by, reported to, or reasonably available to you involving the device or a related device--if, after reviewing the bibliography and summary, CDRH concludes that it needs a copy of the published and unpublished reports, CDRH will notify you that copies of such reports shall be submitted;

(2) written promotional material; and

(3) a description of changes made in the device not previously submitted in a PMA supplement.

Adverse Reaction and Device Defect Reporting. You shall submit 3 copies of a written report to the Food and Drug Administraiton, Center for Devices and Radiological Health (CDRH), 8757 Georgia Avenue, Silver Spring, Maryland 20910 within 10 days after you receive or have knowledge of information about:

(1) a mixup of the device or its labeling with another article;

(2) any significant chemical, physical, or other change or deterioration in the device, or any failure of one or more of the the devices to meet the specifications established in the application;

(3) any adverse reaction, side effect, injury, toxicity, or sensitivity reaction that is attributable to the device; and

(a) has not been addressed by the device's labeling or

(b) has been addressed by the device's labeling, but is occurring with unexpected severity or frequency.

Reporting under the Medical Device Reporting (MDR) Regulation. The Medical Device Reporting (MDR) Regulation became effective on December 13, 1984, and requires that all manufacturers and importers of medical devices, including in vitro diagnostic devices, report to FDA whenever they receive or otherwise become aware of information that reasonably suggests that one of its marketed devices (1) may have caused or contributed to a death or serious injury or (2) has malfunctioned and that the device or any other device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to reoccur.

The conditions of approval accompanying PMA approval orders may require that the same events subject to reporting under the MDR Regulation must also be included in periodic reports to the PMA. FDA has determined that such duplicative reporting is unnecessary. Whenever an event involving a device is subject to reporting under both the MDR Regulation and the conditions of approval for this PMA, you shall submit the appropriate reports required by the MDR Regulation and identified with the PMA reference number to the following office:

Device Monitoring Branch (HFZ-343)
Center for Devices and Radiological Health
Food and Drug Administration
8757 Georgia Avenue
Silver Spring, Maryland 20910
Telephone (301) 427-7500

Copies of the MDR Regulation and a FDA publication entitled, "An Overview of the Medical Device Reporting Regulation", are available by written request to the above address or by telephoning (301) 427-8100.

Note: All conditions of approval are subject to change upon publication of the final order for the premarket approval procedural regulation.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
8757 Georgia Avenue
Silver Spring MD 20910

RECEIVED
JAN 27 1986
R. H. O'HOLLA

JAN 2 3 1986

Mr. Robert H. O'Holla
Director
Regulatory Affairs
Research and Development Division
Ethicon, Inc.
Somerville, New Jersey 08876

Re: N16-374/S29
PROLENE™ Polypropylene
Nonabsorbable Surgical
Suture, USP
Filed: November 29, 1985

Dear Mr. O'Holla:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its evaluation of your premarket approval application (PMA) supplement, which requested approval for the addition of a thermoformed primary suture package as an alternate to the currently approved package. Based on data previously reviewed for this packaging material for similar products and on the information submitted, the PMA supplement is approved subject to the conditions described in the "Conditions of Approval" (enclosed).

You may begin production and marketing of the device as modified by your PMA supplement upon receipt of this letter.

If you have any questions concerning the approval of this supplemental application, please contact Kenneth A. Palmer, Ph.D., at (301) 427-7238.

Sincerely yours,

Carl A. Larson

Carl A. Larson, Ph.D.
Director, Division of Surgical
and Rehabilitation Devices
Office of Device Evaluation
Center for Devices
and Radiological Health

CONDITIONS OF APPROVAL

Approved Labeling. As soon as possible, and before commercial distribution of your device, submit two copies of an amendment to this PMA submission with copies of all approved labeling in final printed form to the Food and Drug Administration (FDA), Center for Devices and Radiological Health, PMA Document Mail Center (HFZ-401), 8757 Georgia Avenue, Silver Spring, Maryland 20910.

Advertisement. No advertisement for this device shall recommend or imply that the device may be used for any use that is not mentioned in the approved labeling for the device. All written promotional material shall include a brief statement of the intended uses of the device and relevent warnings, precautions, side effects, and contraindictions.

Premarket Approval Application (PMA) Supplement. Before making any change that could affect the safety or effectiveness of the device, submit a PMA supplement for review and approval by Center for Devices and Radiological Health (CDRH). Such changes may include, but are not limited to:

(1) new indications for use;

(2) labeling changes;

(3) changes in existing manufacturing facilities, methods or quality control procedures;

(4) the use of a different facility or establishment to manufacture, process, or package the device;

(5) changes in sterilization procedures;

(6) changes in packaging;

(7) changes in the performance or design specification, circuits, parts, components, accessories, ingredients, or physical layout of the device; and

(8) extension of the expiration date of the device based on data obtained under a new or revised testing protocol that has not been approved by CDRH. If the protocol has been approved, the change shall be submitted along with the supporting data in the next periodic report required in the PMA approval order. An approved protocol is one included in FDA guidelines applicable to the device or in a PMA submission for the device for which the approval order granted the expiration dating requested by you. Otherwise, you must submit and obtain CDRH approval of a PMA supplement for an expiration dating protocol.

Changes described below that enhance the safety of the device or safety in the use of the device may be placed into effect before your receipt of a written FDA order approving the PMA supplement provided that:

(1) the PMA supplement and its mailing cover are plainly marked "Special PMA Supplement - Changes Being Effected";

(2) the PMA supplement provides a full explanation of the basis for the changes;

(3) the applicant has received acknowledgement of FDA receipt of the PMA supplement;

(4) the PMA supplement specifically identifies the date that such changes are being effected; and

(5) the changes are among the following:

(a) labeling changes that add or strengthen a contraindication, warning, precaution, or adverse reaction or effect;

(b) labeling changes that add or strengthen an instruction that is intended to enhance the safe use of the device;

(c) labeling changes that delete misleading, false, or unsupported indications; or

(d) changes in the manufacturing process or quality controls that add a new specification or test method, or otherwise provide additional assurance of purity, identity, strength or reliability of the device.

You need submit only three (3) copies of a PMA supplement and include only information relevant to the proposed or effected changes in the device. The submission shall include a separate section that identifies all changes for which approval is being requested. You shall submit additional copies and additional information if requested by CDRH.

FDA may, as experience permits, issue guidelines listing specific types of changes that do not require FDA approval before implementation.

Post-Approval Reports. Continued approval of your device is contingent upon the submission of 2 copies of post-approval reports to the Food and Drug Administration, Center for Devices and Radiological Health, PMA Document Mail Center (HFZ-401), 8757 Georgia Avenue, Silver Spring, Maryland 20910 at intervals of 1 year from the date of this letter. The required contents of these reports will be described in the final order for the premarket approval procedural regulation which will be published in the FEDERAL REGISTER in the future. Until this regulation is published in final form, each periodic report shall consist of information that previously has not been submitted as part of a PMA supplement and which you have obtained since the last post-approval report or since receipt of this letter, whichever is later;

(1) a bibliography and summary of reports in the scientific literature involving the device and unpublished reports of in vitro, animal and clinical experience studies, investigations, and tests conducted by, reported to, or reasonably available to you involving the device or a related device--if, after reviewing the bibliography and summary, CDRH concludes that it needs a copy of the published and unpublished reports, CDRH will notify you that copies of such reports shall be submitted;

(2) written promotional material; and

(3) a description of changes made in the device not previously submitted in a PMA supplement.

Adverse Reaction and Device Defect Reporting. You shall submit 3 copies of a written report to the Food and Drug Administraiton, Center for Devices and Radiological Health (CDRH), 8757 Georgia Avenue, Silver Spring, Maryland 20910 within 10 days after you receive or have knowledge of information about:

(1) a mixup of the device or its labeling with another article;

(2) any significant chemical, physical, or other change or deterioration in the device, or any failure of one or more of the the devices to meet the specifications established in the application;

(3) any adverse reaction, side effect, injury, toxicity, or sensitivity reaction that is attributable to the device; and

(a) has not been addressed by the device's labeling or

(b) has been addressed by the device's labeling, but is occurring with unexpected severity or frequency.

Reporting under the Medical Device Reporting (MDR) Regulation. The Medical Device Reporting (MDR) Regulation became effective on December 13, 1984, and requires that all manufacturers and importers of medical devices, including in vitro diagnostic devices, report to FDA whenever they receive or otherwise become aware of information that reasonably suggests that one of its marketed devices (1) may have caused or contributed to a death or serious injury or (2) has malfunctioned and that the device or any other device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to reoccur.

The conditions of approval accompanying PMA approval orders may require that the same events subject to reporting under the MDR Regulation must also be included in periodic reports to the PMA. FDA has determined that such duplicative reporting is unnecessary. Whenever an event involving a device is subject to reporting under both the MDR Regulation and the conditions of approval for this PMA, you shall submit the appropriate reports required by the MDR Regulation and identified with the PMA reference number to the following office:

Device Monitoring Branch (HFZ-343)
Center for Devices and Radiological Health
Food and Drug Administration
8757 Georgia Avenue
Silver Spring, Maryland 20910
Telephone (301) 427-7500

Copies of the MDR Regulation and a FDA publication entitled, "An Overview of the Medical Device Reporting Regulation", are available by written request to the above address or by telephoning (301) 427-8100.

Note: All conditions of approval are subject to change upon publication of the final order for the premarket approval procedural regulation.

Exhibit 32

TAB

Section 6.

Section 6 Information concerning the quantity of the drug distributed, in a manner and form that facilitates estimates of the incidence of any adverse effects reported to be associated with the use of the drug.

ETHICON, Inc. has marketed in excess of 1,580,000 dozens of PROLENE sutures during this reporting period.

Three (3) patient associated experiences were reported to us during this reporting period. Therefore, the incidence of adverse effects reported to be associated with the use of PROLENE suture is extremely low.

Exhibit 33

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
8757 Georgia Avenue
Silver Spring MD 20910

MAY 23 1986

R. H. O'HOLLA

Mr. Robert H. O'Holla
Director
Regulatory Affairs
Research and Development Division
Ethicon, Inc.
Somerville, New Jersey 08876

Re: N16-374/S30
PROLENE™ Polypropylene
Nonabsorbable Surgical
Suture, USP
Filed: March 21, 1986

Dear Mr. O'Holla:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its evaluation of your premarket approval application (PMA) supplement, which requested approval for the reduction in diameter of the suture tips to facilitate the swaging of finer wire diameter needles. Based on the information submitted, the PMA supplement is approved subject to the conditions described in the "Conditions of Approval" (enclosed).

You may begin production and marketing of the device as modified by your PMA supplement upon receipt of this letter.

If you have any questions concerning the approval of this supplemental application, please contact Kenneth A. Palmer, Ph.D., at (301) 427-7238.

Sincerely yours,

Carl A Larson

Carl A. Larson, Ph.D.
Director
Division of Surgical
and Rehabilitation Devices
Office of Device Evaluation
Center for Devices
and Radiological Health

Enclosure

REVISED MAY 1, 1985

I

CONDITIONS OF APPROVAL

Approved Labeling. As soon as possible, and before commercial distribution of your device, submit two copies of an amendment to this PMA submission with copies of all approved labeling in final printed form to the Food and Drug Administration (FDA), Center for Devices and Radiological Health, PMA Document Mail Center (HFZ-401), 8757 Georgia Avenue, Silver Spring, Maryland 20910.

Premarket Approval Application (PMA) Supplement. Before making any change that could affect the safety or effectiveness of the device, submit a PMA supplement for review and approval by Center for Devices and Radiological Health (CDRH). Such changes may include, but are not limited to:

(1) new indications for use;

(2) labeling changes;

(3) changes in existing manufacturing facilities, methods or quality control procedures;

(4) the use of a different facility or establishment to manufacture, process, or package the device;

(5) changes in sterilization procedures;

(6) changes in packaging;

(7) changes in the performance or design specification, circuits, parts, components, accessories, ingredients, or physical layout of the device; and

(8) extension of the expiration date of the device based on data obtained under a new or revised testing protocol that has not been approved by CDRH. If the protocol has been approved, the change shall be submitted along with the supporting data in the next periodic report required in the PMA approval order. An approved protocol is one included in FDA guidelines applicable to the device or in a PMA submission for the device for which the approval order granted the expiration dating requested by you. Otherwise, you must submit and obtain CDRH approval of a PMA supplement for an expiration dating protocol.

Changes described below that enhance the safety of the device or safety in the use of the device may be placed into effect before your receipt of a written FDA order approving the PMA supplement provided that:

(1) the PMA supplement and its mailing cover are plainly marked "Special PMA Supplement - Changes Being Effected";

(2) the PMA supplement provides a full explanation of the basis for the changes;

(3) the applicant has received acknowledgement of FDA receipt of the PMA supplement;

(4) the PMA supplement specifically identifies the date that such changes are being effected; and

(5) the changes are among the following:

(a) labeling changes that add or strengthen a contraindication, warning, precaution, or adverse reaction or effect;

(b) labeling changes that add or strengthen an instruction that is intended to enhance the safe use of the device;

(c) labeling changes that delete misleading, false, or unsupported indications; or

(d) changes in the manufacturing process or quality controls that add a new specification or test method, or otherwise provide additional assurance of purity, identity, strength or reliability of the device.

You need submit only three (3) copies of a PMA supplement and include only information relevant to the proposed or effected changes in the device. The submission shall include a separate section that identifies all changes for which approval is being requested. You shall submit additional copies and additional information if requested by CDRH.

FDA may, as experience permits, issue guidelines listing specific types of changes that do not require FDA approval before implementation.

Post-Approval Reports. Continued approval of your device is contingent upon the submission of 2 copies of post-approval reports to the Food and Drug Administration, Center for Devices and Radiological Health, PMA Document Mail Center (HFZ-401), 8757 Georgia Avenue, Silver Spring, Maryland 20910 at intervals of 1 year from the date of this letter. The required contents of these reports will be described in the final order for the premarket approval procedural regulation which will be published in the FEDERAL REGISTER in the future. Until this regulation is published in final form, each periodic report shall consist of information that previously has not been submitted as part of a PMA supplement and which you have obtained since the last post-approval report or since receipt of this letter, whichever is later;

(1) a bibliography and summary of reports in the scientific literature involving the device and unpublished reports of in vitro, animal and clinical experience studies, investigations, and tests conducted by, reported to, or reasonably available to you involving the device or a related device--if, after reviewing the bibliography and summary, CDRH concludes that it needs a copy of the published and unpublished reports, CDRH will notify you that copies of such reports shall be submitted;

(2) written promotional material; and

(3) a description of changes made in the device not previously submitted in a PMA supplement.

Adverse Reaction and Device Defect Reporting. You shall submit 3 copies of a written report to the Food and Drug Administraiton, Center for Devices and Radiological Health (CDRH), 8757 Georgia Avenue, Silver Spring, Maryland 20910 within 10 days after you receive or have knowledge of information about:

(1) a mixup of the device or its labeling with another article;

(2) any significant chemical, physical, or other change or deterioration in the device, or any failure of one or more of the the devices to meet the specifications established in the application;

(3) any adverse reaction, side effect, injury, toxicity, or sensitivity reaction that is attributable to the device; and

(a) has not been addressed by the device's labeling or

(b) has been addressed by the device's labeling, but is occurring with unexpected severity or frequency.

Reporting under the Medical Device Reporting (MDR) Regulation. The Medical Device Reporting (MDR) Regulation became effective on December 13, 1984, and requires that all manufacturers and importers of medical devices, including in vitro diagnostic devices, report to FDA whenever they receive or otherwise become aware of information that reasonably suggests that one of its marketed devices (1) may have caused or contributed to a death or serious injury or (2) has malfunctioned and that the device or any other device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to reoccur.

The conditions of approval accompanying PMA approval orders may require that the same events subject to reporting under the MDR Regulation must also be included in periodic reports to the PMA. FDA has determined that such duplicative reporting is unnecessary. Whenever an event involving a device is subject to reporting under both the MDR Regulation and the conditions of approval for this PMA, you shall submit the appropriate reports required by the MDR Regulation and identified with the PMA reference number to the following office:

Device Monitoring Branch (HFZ-343)
Center for Devices and Radiological Health
Food and Drug Administration
8757 Georgia Avenue
Silver Spring, Maryland 20910
Telephone (301) 427-7500

Copies of the MDR Regulation and a FDA publication entitled, "An Overview of the Medical Device Reporting Regulation", are available by written request to the above address or by telephoning (301) 427-8100.

Note: All conditions of approval are subject to change upon publication of the final order for the premarket approval procedural regulation.

Exhibit 34

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
8757 Georgia Avenue
Silver Spring MD 20910

DEC - 3 1986

RECEIVED
DEC - 1986
R. H. O'HOLLA

Mr. Robert H. O'Holla
Director, Regulatory Affairs
Ethicon, Inc.
A Johnson & Johnson Company
Somerville, New Jersey 08876-0151

Re: See Enclosed List
Filed: October 28, 1986

Dear Mr. O'Holla:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its evaluation of your premarket approval application (PMA) supplements, which requested approval for an alternate manufacturing site. Based upon the information submitted, the PMA supplements are approved subject to the conditions described in the "Conditions of Approval" (enclosed).

You may begin production and marketing of the devices as modified by your PMA supplements upon receipt of this letter.

If you have any questions concerning the approval of these supplemental applications, please contact Kenneth A. Palmer, Ph.D., at (301) 427-7238.

Sincerely yours,

Carl A. Larson

Carl A. Larson, Ph.D.
Director, Division of Surgical
and Rehabilitation Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosures

Exhibit 35

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
8757 Georgia Avenue
Silver Spring MD 20910

AUG 28 1987

RECEIVED
AUG 31 1987
R. H. O'HOLLA

Mr. Robert H. O'Holla
Director, Regulatory Affairs
Ethicon, Inc.
Somerville, New Jersey 08876-0151

Re: See Enclosed List
Filed: August 12, 1987

Dear Mr. O'Holla:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its evaluation of your premarket approval application (PMA) supplements, which requested approval for an alternate sterilization process for secondary overwrap packaging. Based upon the information submitted, the PMA supplements are approved subject to the conditions described below and in the "Conditions of Approval" (enclosed). You may begin commercial distribution of the devices as modified by your PMA supplements upon receipt of this letter.

The sale, distribution, and use of these devices are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (act) under authority of section 515(d)(1)(B)(ii) of the act.

Failure to comply with the conditions of approval invalidates this approval order. Commercial distribution of devices that are not in compliance with these conditions is a violation of the Federal Food, Drug, and Cosmetic Act.

All required documents must be submitted in triplicate, unless otherwise specified, to the address below and shall reference the above PMA numbers to expedite processing.

PMA Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
8757 Georgia Avenue
Silver Spring, Maryland 20910

If you have any questions concerning this approval order, please contact Kenneth A. Palmer, Ph.D., at (301) 427-7238.

Sincerely yours,

Carl A. Larson, Ph.D.
Director, Division of Surgical
and Rehabilitation Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

*Trademark

Enclosures

Document Number	Device Name
N85316/S15	ETHILON*/NUROLON* Nylon Sutures Nonabsorbable Surgical Suture, USP
N10389/S25	Catgut Suture (Plain and Chromic) Absorbable Surgical Suture, USP
N11397/S26	Silk Nonabsorbable Surgical Suture, USP
N12815/S22	MERSILENE* Polyester Nonabsorbable Surgical Suture, USP
N14226/S8	Collagen Suture Chromic Absorbable Surgical Suture, USP
N16374/S33	PROLENE* Polypropylene Nonabsorbable Surgical Suture, USP
N17472/S42	VICRYL* (polyglactin 910) Synthetic Absorbable Suture, Dyed
N17804/S37	ETHIBOND* Polyester Nonabsorbable Surgical Suture, USP, Dyed
N18331/S19	PDS* (polydioxanone) Synthetic Absorbable Suture (Dyed)

*Trademark

Exhibit 36

file
56.1

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
8757 Georgia Avenue
Silver Spring MD 20910

OCT - 7 1988

RECEIVED
OCT 13 1988
R. H. O'HOLLA

Mr. James P. O'Donnell
Manager, Regulatory Affairs & Statistics
Ethicon, Inc.
Somerville, New Jersey 08876-0151

RE: N16374/S34
PROLENE* Polypropylene Suture
Clear and Pigmented
Nonabsorbable Surgical Suture, USP
Filed: September 13, 1988

Dear Mr. O'Donnell:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its evaluation of your premarket approval application (PMA) supplement, which requested approval for updated labeling changes for size 7-0 PROLENE* clear and pigmented sutures. Based upon the information submitted, the PMA supplement is approved subject to the conditions described below and in the "Conditions of Approval" (enclosed). You may begin commercial distribution of the device as modified by your PMA supplement upon receipt of this letter.

The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (act) under authority of section 515(d)(1)(B)(ii) of the act.

Failure to comply with the conditions of approval invalidates this approval order. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

All required documents must be submitted in triplicate, unless otherwise specified, to the address below and shall reference the above PMA number to expedite processing.

PMA Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
8757 Georgia Avenue
Silver Spring, Maryland 20910

If you have any questions concerning this approval order, please contact Mr. Kevin J. Crossen, at (301) 427-7238.

Sincerely yours,

Carl A. Larson

Carl A. Larson, Ph.D.
Director, Division of Surgical
and Rehabilitation Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

*Trademark
Enclosure

REVISED: November 19, 1986

CONDITIONS OF APPROVAL

Approved Labeling. As soon as possible, and before commercial distribution of your device, submit two copies of an amendment to this PMA submission with copies of all approved labeling in final printed form to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration (FDA), 8757 Georgia Avenue, Silver Spring, Maryland 20910.

Advertisement. No advertisement and other descriptive printed material issued by the applicant or private label distributor with respect to this device shall recommend or imply that the device may be used for any use that is not included in the FDA approved labeling for the device. If FDA has restricted the sale, distribution and use of the device to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the act under the authority of section 515(d)(1)(B)(ii) of the act, all advertisements and other descriptive printed material issued by the applicant or distributor with respect to the device shall include a brief statement of the intended uses of the device and relevant warnings, precautions, side effects and contraindications.

Premarket Approval Application (PMA) Supplement. Before making any change affecting the safety or effectiveness of the device, submit a PMA supplement for review and approval by FDA unless the change is of a type for which a "Special PMA Supplement-Changes Being Effected" is permitted under 21 CFR 814.39(d) or for which FDA has advised in an advisory opinion or in correspondence in accordance with 21 CFR 814.39(e) that an alternate submission is permitted. A PMA supplement or alternate submission shall comply with applicable requirements under 21 CFR 814.39 of the final rule for Premarket Approval of Medical Devices (51 FR 26342) published in the Federal Register of July 22, 1986.

Postapproval Reports. Continued approval of this PMA is contingent upon the submission of postapproval reports required under 21 CFR 814.84 at intervals of 1 year from the date of approval of the original PMA. Postapproval reports for supplements approved under the original PMA, if applicable, are to be included in the next and subsequent annual reports for the original PMA unless specified otherwise in the approval order for the PMA supplement. Two copies identified as "Annual Report" and bearing the applicable PMA reference number are to be submitted to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 8757 Georgia Avenue, Silver Spring, Maryland 20910. The postapproval report shall indicate the beginning and ending date of the period covered by the report and shall include the following information required by 21 CFR 814.84:

(1) Identification of changes described in 21 CFR 814.39(a) and changes required to be reported to FDA under 21 CFR 814.39(b).

(2) Bibliography and summary of the following information not previously submitted as part of the PMA and that is known to or reasonably should be known to the applicant:

(a) unpublished reports of data from any clinical investigations or nonclinical laboratory studies involving the device or related devices ("related" devices include devices which are the same or substantially similar to the applicant's device); and

(b) reports in the scientific literature concerning the device.

If, after reviewing the bibliography and summary, FDA concludes that agency review of one or more of the above reports is required, the applicant shall submit two copies of each identified report when so notified by FDA.

Adverse Reaction and Device Defect Reporting. As provided by 21 CFR 814.82(a)(9), FDA has determined that in order to provide continued reasonable assurance of the safety and effectiveness of the device, the applicant shall submit 3 copies of a written report identified as an "Adverse Reaction Report" or "Device Defect Report", as applicable, to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 8757 Georgia Avenue, Silver Spring, Maryland 20910 within 10 days after the applicant receives or has knowledge of information concerning:

(1) A mixup of the device or its labeling with another article.

(2) Any adverse reaction, side effect, injury, toxicity, or sensitivity reaction that is attributable to the device and

(a) has not been addressed by the device's labeling or

(b) has been addressed by the device's labeling, but is occurring with unexpected severity or frequency.

(3) Any significant chemical, physical or other change or deterioration in the device or any failure of the device to meet the specifications established in the approved PMA that could not cause or contribute to death or serious injury but are not correctable by adjustments or other maintenance procedures described in the approved labeling. The report shall include a discussion of the applicant's assessment of the change, deterioration or failure and any proposed or implemented corrective action by the applicant. When such events are correctable by adjustments or other maintenance procedures described in the approved labeling, all such events known to the applicant shall be included in the Annual Report described under "Postapproval Reports" above unless specified otherwise in the conditions of approval to this PMA. This postapproval report shall appropriately categorize these events and include the number of reported and otherwise known instances of each category during the reporting period. Additional information regarding the events discussed above shall be submitted by the applicant when determined by FDA to be necessary to provide continued reasonable assurance of the safety and effectiveness of the device for its intended use.

Reporting under the Medical Device Reporting (MDR) Regulation. The Medical Device Reporting (MDR) Regulation became effective on December 13, 1984, and requires that all manufacturers and importers of medical devices, including in vitro diagnostic devices, report to FDA whenever they receive or otherwise become aware of information that reasonably suggests that one of its marketed devices (1) may have caused or contributed to a death or serious injury or (2) has malfunctioned and that the device or any other device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to reoccur.

The "Conditions of Approval" accompanying PMA approval orders may require that the same events subject to reporting under the MDR Regulation must also be included in periodic reports to the PMA. FDA has determined that such duplicative reporting is unnecessary. Whenever an event involving a device is subject to reporting under both the MDR Regulation and the "Conditions of Approval" for this PMA, you shall submit the appropriate reports required by the MDR Regulation and identified with the PMA reference number to the following office:

Device Monitoring Branch (HFZ-343)
Center for Devices and Radiological Health
Food and Drug Administration
8757 Georgia Avenue
Silver Spring, Maryland 20910
Telephone (301) 427-7500

Events included in periodic reports to the PMA that have also been reported under the MDR Regulation must be so identified in the periodic report to the PMA to prevent duplicative entry into FDA information systems.

Copies of the MDR Regulation and an FDA publication entitled, "An Overview of the Medical Device Reporting Regulation", are available by written request to the above address or by telephoning (301) 427-8100.

Exhibit 37

PACKAGE INSERT

SIDE # 1

DATE:

PROLENE.

POLYPROPYLENE SUTURE

Nonabsorbable Surgical Suture, U.S.P.

DESCRIPTION

PROLENE* Polypropylene Suture, U.S.P. (clear or pigmented) is an isotactic crystalline stereoisomer of a linear hydrocarbon polymer containing little or no unsaturation. The pigmented suture contains Copper Phthalocyanine Blue.

ACTIONS

PROLENE Polypropylene Suture, U.S.P. causes a minimal, transient acute inflammatory reaction. This is followed by the formation of a microscopic layer of fibrous tissue around the suture. The suture is not absorbed nor is it subject to degradation or weakening by the action of tissue enzymes.

INDICATIONS

PROLENE Polypropylene Suture, U.S.P. may be used wherever Nonabsorbable Surgical Suture, U.S.P. is recommended. Due to its relative biological inertness, it is recommended for use where the least possible suture reaction is desired. As a true monofilament, PROLENE Polypropylene Suture, U.S.P. resists involvement in infection and has been successfully employed in contaminated and infected wounds to eliminate or minimize later sinus formation and suture extrusion.

Because of its lack of adherence to tissue, PROLENE Polypropylene Suture, U.S.P. is efficacious as a pull-out suture.

CONTRAINDICATIONS

There are no known contraindications.

WARNINGS

Do not resterilize.

*Trademark

PROLENE size 7-0 sutures are U.S.P., except for diameter.

MAXIMUM SUTURE OVERSIZE IN DIAMETER (mm) FROM U.S.P.

U.S.P. SUTURE SIZE DESIGNATION	MAXIMUM OVERSIZE (mm)
7-0	.007

SIDE # 2

PRECAUTIONS

As with any suture, care should be taken to avoid damage when handling. Avoid the crushing or crimping application of surgical instruments, such as needleholders and forceps, to the strand except when grasping the free end of the suture during an instrument tie.

As with other synthetic sutures, knot security requires the standard surgical technique of flat and square ties with additional throws if indicated by surgical circumstance and the experience of the operator.

ADVERSE REACTIONS

Transitory local inflammatory reactions have been reported.

DOSAGE AND ADMINISTRATION

Use as required per surgical procedure.

HOW SUPPLIED

PROLENE* Polypropylene Sutures, pigmented, are available as sterile strands in U.S.P. sizes 11-0 thru 6-0 (metric size 0.1—0.4) and 5-0 thru 2 (metric size 0.7—5.0).

PROLENE Polypropylene Sutures, clear, are available as sterile strands in U.S.P. sizes 6-0 thru 2 (metric size 0.7—5.0).

PROLENE size 7-0 sutures are U.S.P. except for diameter.

PROLENE Polypropylene Sutures, pigmented and clear, in U.S.P. sizes 4-0 thru 2 (metric size 1.5—5) are also available attached to CONTROL RELEASE* removable needles.

PROLENE Polypropylene Sutures, sizes 0 thru 5-0 are also available attached to Teflon† or Dacron† felt pledgets measuring 1/8" x 1/8" x 1/16" (3.0mm x 3.0mm x 1.5mm), 1/4" x 1/8" x 1/16" (7.0mm x 3.0mm x 1.5mm), or 3/8" x 3/16" x 1/16" (9.0mm x 4.0mm x 1.5mm). An additional size for the Dacron Pledget is also available measuring 1/16" x 1/4" x 1/4" (1.5mm x 6.0mm x 6.0mm).

CAUTION: Federal Law restricts this device to sale, distribution and use by or on the order of a physician or a veterinarian.

ETHICON, INC.
a Johnson & Johnson company

Somerville, New Jersey 08876-0151
Made in U.S.A.

*Trademark
389xxx

†TM E.I. DuPont de Nemours & Co.

All PROLENE polypropylene sutures are available in a variety of lengths with and without permanently attached needles.

Exhibit 38

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
1390 Piccard Drive
Rockville, MD 20850

MAR 20 1990

REGULATORY AFFAIRS
MAR 26 1990
RECEIVED

Mr. James P. O'Donnell
Manager
Regulatory Affairs and Statistics
Ethicon, Inc.
P.O. Box 151
Somerville, New Jersey 08876-0151

Re: See Enclosed List
Filed: February 23, 1990

Dear Mr. O'Donnell:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its evaluation of your premarket approval application (PMA) supplements, which requested approval for a change in the release criteria following ethylene oxide secondary sterilization of overwrapped suture packages. Based upon the information submitted, the PMA supplements are approved subject to the conditions described below and in the "Conditions of Approval" (enclosed). You may begin commercial distribution of the devices as modified by your PMA supplements upon receipt of this letter.

The sale, distribution, and use of these devices is restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (act) under authority of section 515(d)(1)(B)(ii) of the act.

Failure to comply with the conditions of approval invalidates this approval order. Commercial distribution of devices that are not in compliance with these conditions is a violation of the act.

All required documents must be submitted in triplicate, unless otherwise specified, to the address below and shall reference the above PMA numbers to expedite processing.

PMA Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
1390 Piccard Drive
Rockville, Maryland 20850

If you have any questions concerning this approval order, please contact Ms. Diane Minear at (301) 427-1090.

Sincerely yours,

Carl A. Larson

Carl A. Larson, Ph.D.
Director
Division of Surgical and
Rehabilitation Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosures

N11397/S28	Silk Suture, Nonabsorbable Surgical Suture, USP
N12815/S24	MERSILENE™ Polyester Suture Nonabsorbable Surgical Suture, USP
N16374/S35	PROLENE™ Polypropylene Suture, Nonabsorbable Surgical Suture, USP
N17804/S39	ETHIBOND™ Polyester Suture Nonabsorbable Surgical Suture, USP
N18331/S22	PDS II (Polydioxanone) Suture, Synthetic Absorbable Suture
N85316/S17	ETHILON™/NUROLON Nylon Sutures Nonabsorbable Surgical Suture, USP

Exhibit 39

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
1390 Piccard Drive
Rockville, MD 20850

JUL 5 1990

Mr. Walter S. Hennig
Vice President, Quality Functions
United States Surgical Corporation
150 Glover Avenue
Norwalk, Connecticut 06856

Re: Reclassification of Nonabsorbable Polypropylene Surgical Suture, Docket Number 88P-0173

Dear Mr. Hennig:

INTRODUCTION

The Center for Devices and Radiological Health (CDRH) for the Food and Drug Administration (FDA) has completed its review of your reclassification petition for the nonabsorbable polypropylene surgical suture. FDA concludes that the generic type of device, nonabsorbable polypropylene surgical suture, and all devices substantially equivalent to this generic type, should be reclassified from class III into class II with a low priority for the development of a performance standard. This order, therefore, reclassifies nonabsorbable polypropylene surgical sutures into class II effective immediately.

FDA identifies the generic type of device the subject of this reclassification, as follows:

> Nonabsorbable polypropylene surgical suture is a monofilament, nonabsorbable, sterile, flexible thread prepared from long-chain polyolefin polymer known as polypropylene and is indicated for use in soft tissue approximation. The polypropylene surgical suture meets USP requirements as described in the USP Monograph for Nonabsorbable Surgical Sutures; it may be undyed or dyed with an FDA approved color additive; and the suture may be provided with or without a standard needle attached.

As you know, on May 4, 1988, FDA filed the reclassification petition submitted by Advanced Biosearch Associates of Danville, California on your behalf requesting reclassification of nonabsorbable polypropylene surgical suture from class III into class II. The petition was submitted under section

520(1) of the Federal Food, Drug and Cosmetic Act ("act"), 21 U.S.C. 360j(1), seeking reclassification under the procedures set forth in section 520(1)(2) of the act, 21 U.S.C. 360j(1)(2), and 21 CFR 860.136 of the agency's regulations.

Consistent with the act and the regulations, the agency consulted with the General and Plastic Surgery Devices Panel ("Panel") regarding the reclassification petition. The agency, by its September 28, 1988 letter and statements at the panel meeting, fully briefed the Panel about its obligations regarding the reclassification petition for nonabsorbable polypropylene surgical suture that was before it. The Panel, during an open public meeting on October 20, 1988, recommended that FDA reclassify nonabsorbable polypropylene surgical suture from class III into class II, and that FDA assign a high priority to the development of a performance standard for the generic type of device under section 514 of the act, although a performance standard need not be in place before reclassification is effective (Ref. 8 at page 55).

After reviewing all data in the petition and presented before the Panel, and after fully considering the Panel's recommendation and the views of the participants at the panel meeting, FDA, based on the information set forth in this letter, is ordering the reclassification of the generic type of device, identified on page 1, supra, from class III to class II.

RECLASSIFICATION PROCEDURE

Reclassification of nonabsorbable polypropylene surgical suture is governed by section 520(1) of the act, 21 U.S.C. 306j(1). The nonabsorbable polypropylene surgical suture is regulated as a class III device because prior to the Amendments it was subject to an approved "new drug" application submitted under section 505(b). See Section 520(1)(1)(A). Devices subject to "new drug" approvals prior to the Amendments are known as transitional devices and are automatically placed into class III to assure continuity of regulation.

Section 520(1)(1)(D), likewise, automatically classifies into class III a device that is "within a type of device described in subparagraph (A), (B), or (C) [of section 520(1)(1)] and is substantially equivalent to another device within that type." No time or other limitations narrow the scope of section 520(1)(1), nor is it suggested by the statute's text that anything other than all devices that fit within the scope of section 520(1)(1) are to be considered transitional, class III devices. Therefore, nonabsorbable polypropylene surgical sutures that are introduced well after the enactment date of the Amendments, which are substantially equivalent to a suture classified under section 520(1)(1)(A), are classified into class III under the authority of section 520(1)(1)(D).

Section 520(1)(2) of the act, which sets forth the procedures for reclassification of devices classified under section 520(1)(1), unambiguously applies to all devices classified under that section, and its scope is no more limited than that of section 520(1)(1). The statute's language is clear that section 520(1)(2) of the act is the exclusive means for reclassifying a device

classified under section 520(l)(1). Nothing in the act suggests that transitional device reclassification should be initiated under any section of the act other than section 520(l)(2).

The act's premarket notification requirement demonstrates further that this proceeding is authorized by the transitional device reclassification provisions. If any person were to file a premarket notification under section 510(k) of the act, 21 U.S.C. 360(k), he would be required to identify:

> The class in which the device is classified under section 513 or if such person determines that the device is not classified under such section, a statement of that determination and the basis for such person's determination that the device is or is not so classified (emphasis added). Id.

Clearly, nonabsorbable polypropylene surgical suture was not classified under section 513. Congress, as evidenced by the underlined portion of the above-quoted language, recognized that classification could occur outside of section 513. Section 520(l)(1) provides the only means of classifying a device outside of section 513 available under the act, and nonabsorbable polypropylene surgical suture was classified under the authority of that section. Accordingly, any person now bringing nonabsorbable polypropylene surgical suture to the market for the first time would be required to inform the agency in the context of section 510(k) of whether his nonabsorbable polypropylene surgical suture is substantially equivalent to a preamendment suture, as classified under section 520(l)(1), or a unique and, therefore, "new" suture as classified under section 513(f)(1).

For the nonabsorbable polypropylene surgical suture the subject of this reclassification proceeding, it is unchallenged that it was classified into class III under section 520(l)(1). Accordingly, since neither sections 520(l)(1) nor 520(l)(2) express any time restraints or other limitations regarding the acts of classification or reclassification of transitional devices, and since the Amendments, through premarket notification, intend that substantially equivalent devices, including transitional devices, be classified the same, I must conclude that the agency's position, that section 520(l)(2) describes the reclassification procedures for devices originally classified under section 520(l)(1), is reasonable and should be followed.[1]

---

[1] The agency's understanding of the transitional device provision is consistent with the act and the agency's regulations, and is also supported by legislative history, stating:

> [the] [o]pportunity to petition [under the transitional device provisions] for reclassification to class II or I is afforded the manufacturer or importer of any device classified into class III as a result of [section 520(l)(1).]

H.R. Rep. No. 853, 94th Cong., 2d Sess., February 29, 1976 at 38.

As the above discussion demonstrates, Congress intended to permit persons, who for the first time desire to manufacture or import transitional devices, the opportunity to seek reclassification under section 520(1)(2), notwithstanding the fact that reclassification was sought well after the passage of the Amendments. Moreover, U.S. Surgical, in our view and as the record shows, is an appropriate party to petition for reclassification under section 520(1)(2) in that the company intends to market nonabsorbable polypropylene surgical suture, and presently has received approval from FDA to export nonabsorbable polypropylene surgical suture to Italy, West Germany, France, The Netherlands and Switzerland (Ref. 150). Under these circumstances, U.S. Surgical, like any person submitting a premarket notification under section 510(k) seeking classification under section 520(1)(1), has standing to pursue reclassification under section 520(1)(2) from an automatic class III placement.

DECISION

After reviewing the publicly available literature in the record, the Panel's deliberation, and FDA's past actions regarding nonabsorbable polypropylene surgical suture, it is apparent to FDA that a class III designation for nonabsorbable polypropylene surgical suture constitutes overregulation.

By limiting the generic class, the subject of this order, to nonabsorbable polypropylene surgical suture, as defined on page 1, FDA, according to the record evidence, has limited this reclassification to nonabsorbable polypropylene surgical suture with the same or similar health risks. This approach is entirely consistent with FDA's definition of a generic type of device, see 21 CFR 860.3(i), and its view that "[t]he similarity of health risks is fundamental to the concept of classification by generic type of device," see 43 Fed. Reg. 32989, 32992 (July 28, 1978).

Additionally, U.S. Surgical has provided information in its petition to show that, despite variations in nonabsorbable polypropylene surgical suture materials and manufacturing processes, test methods exist to demonstrate whether any nonabsorbable polypropylene surgical suture is within the scope of the generic type of device identified in this order. Therefore, we believe that the nonabsorbable polypropylene surgical suture is well characterized and an appropriate candidate for reclassification.

As you have demonstrated, class II controls are appropriate to regulate nonabsorbable polypropylene surgical suture. Class II controls are indicated where class I controls alone are inadequate to reasonably assure a device's safety and effectiveness, and sufficient information exists to establish a performance standard to provide for such an assurance. See section 513(a)(1)(B) of the act, 21 U.S.C. 360c(a)(1)(B). As our discussion below demonstrates, the publicly available valid scientific evidence contained in the administrative record in this matter identifies the performance parameters and risks that define the safety and effectiveness of nonabsorbable polypropylene surgical suture. Also, valid scientific evidence in the record demonstrates the basis of a performance standard to control these parameters and risks and, thus, "sufficient information to establish a performance

standard," (see section 513(a)(1)(B)), exists to classify nonabsorbable polypropylene surgical suture into class II.

A class II classification may occur with or without an actual standard being in place. Of importance is the fact that enough is known about the performance of nonabsorbable polypropylene surgical suture that the generic premarket clearance criteria of a performance standard constitute a more appropriate level of regulatory control than the agency's product by product premarket review, mandated by class III controls. Indeed, the data in the record show that when weighing benefits to the probable risk of illness or injury resulting from the use of nonabsorbable polypropylene surgical suture, class III controls are unnecessary to assure the device's safe and effective performance.

In granting your petition, FDA has relied on valid scientific evidence, as defined by 21 CFR 860.7(c)(2). The agency's regulations prescribe various types of evidence that may be valid scientific evidence, including, for example, well-controlled studies and reports of significant human experience with marketed devices. Although a well-controlled investigation is a component of valid scientific evidence, it is important to appreciate that such an investigation is but one type of evidence that can be relied upon by FDA to make classification and other regulatory decisions.

FDA firmly believes that end-product test methods are available to thoroughly evaluate nonabsorbable polypropylene surgical suture, and that publicly available valid scientific evidence supports this conclusion. The agency contrues section 514 of the act to sanction the use of end-product testing as a means of evaluating the properties and performance of a device. In that nonabsorbable polypropylene surgical suture is considered by the agency to be well characterized, and the record evidence supports this conclusion, and since valid scientific evidence shows the applicability of various end-product tests to the use of the suture in humans, we believe that class II controls provide a reasonable means, consistent with the act's purpose, to regulate nonabsorbable polypropylene surgical suture.

SCIENTIFIC BASIS

Suture Characterization

By definition, the nonabsorbable polypropylene surgical suture is well characterized. The suture is a monofilament, nonabsorbable, sterile, flexible thread prepared from long-chain polyolefin polymer known as polypropylene and is indicated for use in soft tissue approximation. The polypropylene surgical suture meets USP requirements as described in the USP Monograph for Nonabsorbable Surgical Sutures; it may be undyed or dyed with an FDA approved color additive; and the suture may be provided with or without a standard needle attached.

The nonabsorbable polypropylene surgical suture manufacturing process begins with production of the isotatic form of the polypropylene polymer wherein the attached methyl groups are arranged in a stereoregular

configuration along one side of the "plane" described by a zig-zag carbon chain. It is produced in a solvent polymerization, using hydrocarbon solvent under pressure, at high temperatures and in the presence of a Zeigler-Natta catalyst which promotes the formation of the stereoregular isotatic form of the polypropylene polymer. The resulting insoluble isotatic polymer resin is subsequently purified by filtration and extraction to remove the catalyst, and then dried. Nonabsorbable polypropylene surgical suture may be left undyed (natural), or if desired, dyed with an FDA listed color additive in accordance with section 706 of the act.

The polypropylene resin is extruded at high temperature into polymer fibers of uniform diameter, and a specific multiple of their length are drawn or stretched to provide the necessary tensile properties. Nonabsorbable polypropylene surgical suture is ordinarily monofilamentous, and depending upon the final suture size desired, fibers of appropriate diameter and characteristics are produced. The processed thread is then cut to length, gauged to ensure uniform diameter and tensile strength in accordance with the requirements of United States Pharmacopeia (USP), appropriately packaged (with or without an attached needle), and sterilized to produce a finished suture (Refs. 7, 9, 29, 32, 65, 105, 133, 134 and 135).

Record data show that nonabsorbable polypropylene surgical suture's performance parameters and uses are well documented and understood, and that the generic type of device presents a reasonably uniform risk/benefit profile. Indeed the characteristics and composition of polypropylene are well-defined (Refs. 23, 24, 57, 58, 69, 72, 90, 91, 95, 113, 117, 120, 121, 126, 128-131, 134 and 135). Moreover, the performance parameters of existing nonabsorbable polypropylene surgical suture are well established (Refs. 9, 24, 29, 45, 50, 64, 121, 133, 134, 135 and 137) and the record shows the reasonably safe and effective use of nonabsorbable polypropylene surgical suture in humans (Refs. 17, 21, 33, 41, 42, 87, 95, 120 and 138).

The end product, given its indications for use, must have certain tensile strength characteristics (Refs. 9, 23, 28, 30, 34, 64, 74, 85, 89, 90, 91, 95, 113, 117, 120, 121, 126, 128, 129, 130, 133, 137 and 142). USP sutures, evaluated by uniform end-product testing, will perform successfully, notwithstanding different manufacturing processes (Refs. 7, 9, 64, 137, 24, 85, 133, 134 and 135), and will, among other things, have uniform tensile strengths. Since record data show that all nonabsorbable polypropylene surgical sutures present similar risks and performance characteristics (Refs. 9, 24, 29, 45, 50, 64, 121, 133, 134, 135 and 137), end product testing, in conjunction with other controls, will provide an appropriate means of reasonably assuring safe and effective nonabsorbable polypropylene surgical sutures.

In sum, the principal materials used to produce nonabsorbable polypropylene surgical suture is isotatic polypropylene polymer, and the physical characteristics of these polypropylene polymers are well understood. The USP Standard (Ref. 133 a-l), the American Society for Testing and Materials (ASTM) standards (Ref. 9 a-t) and other state-of-the-art test methods exist to evaluate and analyze the manufacturing process, composition, and physical, mechanical and biological properties of any nonabsorbable

polypropylene surgical suture (Refs. 28, 30, 34, 88, 92, 110, 112, 113, 116-119, 130, 132 and 138). Nonabsorbable polypropylene surgical sutures present the same risks and performance parameters and can be standardized by end-product tests, and are regulable by the same or similar controls. Accordingly, the record shows that nonabsorbable polypropylene surgical suture constitutes a well characterized generic type of device.

Control of Suture Performance

The parameters that need control to provide reasonable assurance of safety and effectiveness for nonabsorbable polypropylene surgical suture are suture breakage, tissue inflammatory response, infection, and suture-related calculogenesis. A discussion of each parameter and the appropriateness of a class II classification for nonabsorbable polypropylene surgical suture, as supported by valid scientific evidence, follows.

1. Suture Breakage

The most important function of a suture is to successfully hold tissue together until healing is sufficiently complete so as to negate the need of the suture. Failure of a suture prior to a wound regaining adequate strength may result in wound dehiscence: a disruption of apposed wound surfaces, interfering with the normal healing process. Suture breakage may occur where there is premature loss of tensile strength (Refs. 4, 23, 29, 32, 42, 43, 44, 64, 70, 83, 90, 95, 115, 117, 121, 126, 128, 129, 130 and 149), due to unfavorable physiological wound site conditions (Refs. 11, 17, 18, 22, 33, 48, 66, 68, 74, 79, 80, 87, 102, 121 and 137), poor surgical technique (Refs. 11, 21, 66, 74, 77, 80, 83, 102, 107, 108, 109, 115, 117, 121 and 137), or improper use of the suture (id.). Importantly, the cumulative risk of nonabsorbable polypropylene surgical suture breakage is small, and its ability to function properly is uncontested.

The data in the record reveal that the incidence of wound dehiscence varies according to a number of factors, not all of which relate to suture breakage (Refs. 11, 17, 18, 48, 54, 66, 68, 74, 80, 81, 87, 107, 108, 109, 121 and 137). Of those wounds that dehisce, only a small fraction are attributable to suture breakage (Refs. 11, 17, 22, 48, 66, 74, 79, 109 and 121). It has also been shown that the incidence of wound dehiscence due to suture breakage occurs infrequently with nonabsorbable polypropylene surgical suture (Refs. 11, 22, 66, 74, 79, 108 and 109), and that the overall incidence of wound dehiscence with nonabsorbable polypropylene surgical suture is low (Refs. 22, 41, 68, 74, 79, 87 and 109).

The loss of tensile strength leading to suture breakage is a potential cause of failure of nonabsorbable polypropylene surgical suture in certain applications (Refs. 4, 32, 42, 70, 115 and 149). Retention of the suture's tensile strength is critical to the function of nonabsorbable polypropylene surgical suture. The record data show that the loss of tensile strength in vivo is primarily related to the oxidative degradation of the polypropylene polymer (Refs. 4, 29, 32, 42, 43 and 44) and that the polymer's degradation proceeds slowly and is generally not considered clinically significant under most circumstances of use (Refs. 1, 4, 42, 121 and 149). The rate and extent

of oxidative degradation vary according to exposure to ultraviolet radiation, and may make the use of the suture in the eye questionable (Refs. 4, 32, 42, 70 and 149). Oxidative enzyme activity and the type of tissue at the wound site, e.g., actively metabolizing tissues, tissues with high oxygen concentration, and inflammation may also contraindicate the suture for certain applications (Refs. 4, 32, 42, 43, 44, 70 and 149).

The patient's health and response to the suture material may affect wound healing (Refs. 11, 17, 18, 48, 66, 74, 80, 81, 87, 107, 108, 109 and 121). Patients whose health has been compromised or weakened by poor nutrition, advanced age, obesity, uncontrolled diabetes, infection, anemia, or with certain forms of cancer, may exhibit delayed wound healing (Refs. 11, 17, 18, 48, 66, 74, 80, 81, 87, 107, 108, 109 and 121) which may increase the likelihood of suture failure. Although some of these factors have been shown experimentally to delay increases in wound strength, a nonabsorbable suture, such as nonabsorbable polypropylene surgical suture, may be preferred over absorbable sutures due to the suture's continuous support of tissues (Refs. 17, 48, 66, 74, 108, 121 and 137).

The appropriate use of nonabsorbable polypropylene surgical suture is important in defining its performance. The record shows that nonabsorbable polypropylene surgical suture has been successfully used in various wound sites and conditions in humans (Refs. 17, 21, 33, 41, 42, 87, 95, 120 and 138). Although, wound dehiscence is most significant in wound closures involving sites which can undergo expansion, stretching, or distention, such as the abdomen, chest, and joints, nonabsorbable polypropylene surgical suture may be the suture of choice due to its continued support of tissues (Refs. 11, 17, 18, 22, 33, 48, 66, 74, 79, 80, 81, 87, 102, 108, 121 and 137). Using nonabsorbable polypropylene surgical suture to close certain wounds has documented advantages related to the physical properties of the suture (Refs. 11, 22, 33, 66, 74, 79, 80, 81, 87, 108 and 121).

Surgical technique also affects the performance of sutures, including nonabsorbable polypropylene surgical suture. Improper closure technique can result in tissue separation and failure of the wound to heal. The factors relating to the wound closure technique that contribute to wound dehiscence include the tightness with which sutures are tied, suture knot security, the adequacy of tissue bites to allow for adequate wound expansion due to distention and damage to the suture during placement (Refs. 11, 17, 18, 21, 23, 48, 57, 58, 64, 66, 69, 74, 77, 79, 83, 87, 95, 102, 107, 108, 109, 115, 117, 120, 121, 129 and 130).

The critical parameter of tensile strength can be controlled by standard in vitro test methods and animal testing. The tensile strength of nonabsorbable polypropylene surgical suture before implantation and after explantation may be measured in a motor-driven tensile strength machine using equipment and procedures described in the USP (Refs. 133, 134 and 135). Moreover, various American Society for Testing and Material (ASTM) tests to evaluate suture strength exist and include, for example, yarn breaking load, breaking tenacity in loop/knot configuration, single textile fiber tensile strength, and in vitro strength loss and material degradation tests (Refs. 9, 134 and 135). Finally, to determine the effects of implantation of

nonabsorbable polypropylene surgical suture upon tensile strength, various in vitro and in vivo methods used by Salthouse (Refs. 116 and 117), Postlethwait (Ref. 110), and others (Refs. 30, 64, 128, 129 and 130), which compare the tensile strength of various absorbable and nonabsorbable sutures, show a suture's performance characteristics.

The various evaluative methods included in the above references are applicable to the safe and effective use of nonabsorbable polypropylene surgical suture in humans in that sutures that have been successfully used in humans are routinely evaluated with these evaluative methods (Refs. 17, 21, 33, 41, 42, 87, 95, 120 and 138). Importantly, the time necessary for wound healing in various sites in humans is known (Refs. 2, 3, 5, 6, 13, 14, 19, 20, 24, 25, 27, 38, 39, 49, 50, 52, 60, 61, 63, 74, 75, 76, 77, 78, 98, 101, 103, 107, 114, 116, 121, 124, 127, 137 and 143), and the above methods permit a determination of whether sufficient suture tensile strength will be present over time to assure a successful result at any given wound site.

Also, many of the above-identified performance parameters and risks can be adequately controlled by labeling disclosures which may be incorporated into a class II standard or required by the class I misbranding controls, which include, among other things, the requirement of adequate directions for use. Disclosures can be made which contain warnings against the use of nonabsorbable polypropylene surgical suture in certain conditions, such as intracamerally in the eye. Also, risks may be avoided by disclosing in labeling that users must be familiar with surgical procedures and techniques involving nonabsorbable polypropylene surgical suture before using it to close wounds.

2. Tissue Inflammatory Response

A tissue inflammatory response is an acute or chronic, localized reaction. Many factors may cause a tissue inflammatory response, including trauma attributed to the implantation of a suture, (Refs. 17, 29, 50, 66, 89, 110, 116, 117, 121, 125, 126 and 137), and foreign body reactions to the suture material (Ref. 74, 87, 107, 119, 121, and 123).

Various studies have documented that an early tissue inflammatory reaction results from the trauma of inserting sutures and does not occur as a result of a reaction to suture material (Refs. 82, 84 and 144). When the suture is placed within tissue with little or no trauma, no inflammatory cell response results, suggesting the conclusion that the body's nonspecific response to tissue injury induces the appearance of inflammatory cells usually seen immediately after suturing (Refs. 31, 87, 107, 119, 146 and 147). The initial reaction of tissues after suturing reflects the amount of injury inherent in the process, and that injury typically is the same for all sutures 5 to 7 days after suturing (Refs. 17, 111, 121, 126, 127 and 137).

The inflammatory response observed beyond 5 to 7 days postoperatively is dependent upon the nature of the specific suture material employed. Specifically, synthetic materials elicit a lesser response than sutures of natural origin (Refs. 29, 110, 116, 117, 119, 121 and 136), and nonabsorbable polypropylene surgical sutures elicit a milder response than absorbable

sutures (Refs. 37, 89, 119, 126, 127 and 137). Additionally, fine gauge sutures provoke a lesser response than large diameter sutures because of their lesser mass and therefore lesser amount of implanted foreign material (Refs. 50 and 136).

Record data show that nonabsorbable polypropylene surgical suture elicits a very mild chronic inflammatory response (Refs. 29, 89, 110, 116, 117, 119, 121, 126, 127 and 137), and because it is ordinarily monofilmentous, this response is among the most benign elicited by any suture material (Ref. 110). Following the initial inflammatory phase, a mild chronic tissue response to nonabsorbable polypropylene surgical suture is seen which is typically characterized by gradual formation of a fibrous encapsulation of the suture with little or no persistent cellular response (Refs. 87, 107, 119, 146 and 147). The chronic tissue inflammatory response to nonabsorbable polypropylene surgical suture is observed to be mild, and less than that elicited by certain other sutures (Refs. 87, 107, 119, 146 and 147) even though the chronic inflammatory response to nonabsorbable polypropylene surgical suture may be associated with granuloma formation in certain circumstances and wound sites (Refs. 74, 87, 107, 119, 121 and 123).

Because of the biocompatability of the synthetic polypropylene material, nonabsorbable polypropylene surgical suture has not been associated with allergic and antigenic reactions. Although the manufacturing process may introduce impurities and residues that can cause tissue inflammatory response, numerous well-established biocompatibility tests provide methods to evaluate a suture's inflammatory potential, including USP tests for impurities and residues, or other state-of-the-art analytical methods (Refs. 8, 9, 10, 12, 51, 53, 62, 65, 72, 86, 93, 96, 97, 104, 106, 112, 132, 133, 134, 145 and 148).

In summary, the risk of early tissue inflammation resulting from trauma is related to the user technique and is no greater for nonabsorbable polypropylene surgical suture than for other suture material. Further, the foreign body response to nonabsorbable polypropylene surgical suture is mild in nature and, therefore, the suture in some circumstances may be preferred to other nonabsorbable sutures. Appropriate labeling disclosures related to tissue inflammation may indicate that all nonabsorbable sutures present an inflammatory response and that nonabsorbable polypropylene surgical suture is less pronounced than that of other nonabsorbable sutures. Moreover, to the extent the manufacturing process may cause residues that introduce a potential for allergic or antigenic reaction, which otherwise is not present with the nonabsorbable polypropylene surgical suture, well-established biocompatibility tests, as part of a standard, exist to evaluate the suture's inflammatory potential.

3. Infection

Although polypropylene surgical suture is manufactured and marketed as a sterile device in accordance with voluntary standards for sterility (Refs. 7, 9, 133 and 134), it, nonetheless, may exacerbate the effects of an existing wound infection, because of its composition, physical configuration, and duration of contact with tissue (Refs. 15, 16, 29, 31, 35, 36, 40, 45, 48, 50,

55, 56, 66, 73, 122, 123, 125, 127 and 141). It has been established that the presence of suture material in a wound increases the wound's susceptibility to infection where the suture serves as a conduit for the mechanical transport of bacteria (Refs. 15, 29, 31, 36, 40, 50, 55, 66, 73, 108, 123, 125, 127, 136 and 139). Also, materials which permit the adherence of the largest amount of bacteria cause the greatest degree of post-surgical infection (Refs. 31, 36, 56, 73 and 125). Indeed, a comparative study of 10 sutures demonstrates that the physical configuration and chemical nature of various suture materials, their coating mechanisms, and the duration of contact between the sutures and bacteria, contribute to the bacterial adherence of the suture. (Ref. 31). The physical configuration of suture material is found to correlate positively with the degree to which sutures aggravate infected wounds (id.), and the use of suture coatings do not appear to reduce the suture-related infection rate (Refs. 36, 45, 50, 55, 123 and 127).

In the presence of infection or contamination, all sutures appear to potentiate the wound infection (Refs. 29, 45, 48, 50, 123 and 127). While nonabsorbable polypropylene surgical suture is not unique in its potential to exacerbate infection, it does appear to carry a somewhat lesser risk than other sutures in this regard (Refs. 16, 32, 40, 55, 95, 121, 123, 126, 138 and 170). The choice of suture material may, therefore, be critical when closing a wound in the presence of infection or potential infection. Because the nonabsorbable polypropylene surgical suture presents somewhat of a lesser risk than other sutures to potential infection, it is a suture of choice for infected wounds or contaminated wounds that present a substantial risk of infection (Refs. 16, 29, 32, 35, 40, 45, 48, 55, 73, 95, 123, 126, 138, 139, 140 and 141).

In summary, since suture selection may be a critical factor in avoiding the exacerbation of an infection, adequate labeling for the nonabsorbable polypropylene surgical suture, as part of a standard, could state that it is a suture of choice in closing infected or contaminated wounds.

4. Calculogenesis

Nonabsorbable polypropylene surgical suture, like other suture material, has been shown to be a nidus for calculogenesis when in contact with salt solutions of the bladder and biliary tract (Refs. 47, 66, 107 and 137). Calculi formation occurs on other natural and synthetic sutures in the bladder, and calculi formation appears to be dependant on the length of time the suture is in contact with urine in the bladder (Refs. 18, 47, 107, 117, and 137). Studies also report that nonabsorbable polypropylene surgical suture, and other sutures, when exposed to salt solutions in the common bile duct have been associated with stone formation (Refs. 18, 60 and 137).

The risk of calculogenesis resulting from implantation of nonabsorbable polypropylene surgical suture in either the urinary or biliary tract is related to the length of time the suture is in contact with a salt solution in those tracts. The risk of calculogenesis with nonabsorbable polypropylene surgical suture is typical of that associated with all nonabsorbable sutures. Thus, adequate labeling as part of a standard, can control this risk by stating that it is inadvisable to place nonabsorbable polypropylene surgical

suture, or for that matter, any suture, in contact with salt solutions in the body's urinary and biliary tracts.

Based on the information presented above, it can be concluded that nonabsorbable polypropylene surgical suture is well characterized and that there is sufficient publicly available valid scientific evidence to demonstrate that a performance standard can be established and used, in combination with the general controls, to provide reasonable assurance of the safety and effectiveness of nonabsorbable polypropylene surgical suture. For control of suture breakage, in particular, for control of suture tensile strength, a standard can assure device safety and effectiveness. See pages 8-9. Likewise, suture-related tissue inflammatory response can be controlled by a performance standard. See page 10.

The act's general controls also make a substantial contribution to the regulation of nonabsorbable polypropylene surgical suture. Manufacturing processes for nonabsorbable polypropylene surgical suture are and will be subject to FDA's Good Manufacturing Practice regulations, and the act's adulteration provisions. Moreover, labeling warnings and disclosures identified throughout this order will provide sufficient control of various nonabsorbable polypropylene surgical suture-related performance parameters or risks to reasonably assure the suture's safe and effective use.

PRIORITY FOR THE DEVELOPMENT OF A STANDARD

While valid scientific evidence demonstrates that a performance standard may be written to control the material, composition, and physical characteristic of this generic type of device in order to reasonably assure its safety and effectiveness, one is not immediately needed. Existing devices, within the generic type covered by this order, typically conform to voluntary standards, including USP standards for nonabsorbable surgical suture. Moreover, nonabsorbable polypropylene surgical suture, as currently manufactured, has established a reasonable record of safe and effective use. The basic properties, principles of manufacture, and appropriate indications and contra-indications for use of nonabsorbable polypropylene surgical suture are well-established, both scientifically and clinically, as documented in publicly available information contained in the petition (Refs. 28, 39, 63, 64, 75, 76, 90, 98, 107, 121, 126 and 134).

In this matter, significant publicly available information indicates that existing nonabsorbable polypropylene surgical sutures are generally safe and effective (Refs. 24, 29, 39, 63, 75, 76, 80, 85, 98, 107, 110, 117, 121 and 127). Thus, FDA concludes that development of a mandatory performance standard is not immediately necessary to protect the public health.

State-of-the-art test methods are well-established to evaluate and analyze the structure, composition, physical, chemical, mechanical, physicochemical and biological properties of any nonabsorbable polypropylene surgical suture to allow a precise determination to be made of the relative safety and effectiveness of marketed nonabsorbable polypropylene surgical sutures and those intended for commercial distribution. Thus, the determination of

comparable safety and effectiveness of future nonabsorbable polypropylene surgical suture and marketed sutures can be made in the context of a premarket notification under section 510(k) of the act, 21 USC 360(k).

FDA, therefore, respectfully disagrees with Panel's recommendation that the promulgation of a mandatory performance standard be a high priority. FDA concludes that development of a mandatory performance standard should be a low priority because the establishment of a regulatory standard is not immediately necessary to protect the public health.

CONCLUSION

Based on the information provided in the petition and presented at the panel meeting, and the information submitted to the administrative record, FDA concludes that the generic type of device, nonabsorbable polypropylene surgical suture, should be reclassified from class III to class II with a low priority for the development of a performance standard.

Sincerely yours,

Robert L. Sheridan
Director
Office of Device Evaluation
Center for Devices
and Radiological Health

Enclosure: References

cc: Howard R. Asher
President
Advanced Biosearch Associates
3880 Blackhawk Road
Danville, California 94526-4617

Enclosure

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d.	#D	2101-82	Standard Test Methods for Tensile Properties of Single Man-Made Textile Fibers Taken From Yarns and Tows
e.	#D	2256-80	Standard Test Method for Breaking Load (Strength) and Elongation of Yarn by the Single Strand Method
f.	#D	2257-80	Standard Test Method for Extractable Matter in Yarns
g.	#D	2259-85	Standard Test Methods for Shrinkage of Yarns in Boiling Water or Dry Heat
h.	#D	3217-79	Standard Test Methods for Breaking Tenacity of Man-Made Textile Fibers in Loop or Knot

			Configurations
i.	#D	3412-86	Standard Test Methods for Coefficient of Friction, Yarn to Yarn
j.	#D	3822-82	Standard Test Method for Tensile Properties of Single Textile Fibers
k.	#F	469-78	Standard Practice for Assessment of Compatibility of Nonporous Polymeric Materials for Surgical Implants With Regard to Effect of Materials on Tissue
l.	#F	719-81	Standard Practice for Testing Biomaterials in Rabbits for Primary Skin Irritation
m.	#F	720-81	Standard Practice for Testing Guinea Pigs for Contact Allergens: Guinea Pig Maximization Test
n.	#F	748-82	Standard Practice for Selecting Generic Biological Test Methods for Materials an Devices
o.	#F	749-82	Standard Practice for Evaluating Material Extracts by Intracutaneous Injection the Rabbit
p.	#F	750-82	Standard Practice for Evaluating Material Extracts by Systematic Injection in the Mouse
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133. United States Pharmacopeia, Revision XXI, 1985:

a. Physical Tests, <621> Chromatography
b. Physical Tests, <761> Nuclear Magnetic Resonance
c. Physical Tests, <851> Spectrophotometry and Light-Scattering
d. Physical Tests, <861> Sutures - Diameter
e. Physical Tests, <871> Sutures - Needle Attachment
f. Physical Tests, <881> Tensile Strength
g. Physical Tests, <661> Containers, Biological Tests -Plastics
h. Biological Tests, <85> Bacterial Endotoxins Test
i. Biological Tests, <71> Sterility

134. United States Surgical Corporation's Reclassification Petition. Docket No. 88P-0173

135. United States Surgical Corporation's letter dated May 15, 1989

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150. Letters from FDA to United States Surgical Corporation granting export rights of nonabsorbable polypropylene surgical suture to The Netherlands, Italy, France, Switzerland and West Germany.

Exhibit 40

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
1390 Piccard Drive
Rockville, MD 20850

OCT 12 1990

Mr. James P. O'Donnell
Manager
Regulatory Affairs
Ethicon, Inc.
P.O. Box 151
Somerville, New Jersey 08876-0151

REGULATORY AFFAIRS
OCT 15
RECEIVED

Re: N16374
PROLENE™, Polypropylene Nonabsorbable Suture

Dear Mr. O'Donnell:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) reclassified the nonabsorbable poypropylene surgical suture on July 5, 1990, effective on that date, from Class III into Class II (order enclosed). Notice of this reclassification will be announced in a future Federal Register notice. This letter constitutes notification that devices approved for commercial distribution under your PMA, N16374 and supplements 1 through 35, of your PMA, have also been reclassified into Class II.

FDA identified nonabsorbable polypropylene surgical suture as follows:

> Nonabsorbable polypropylene surgical suture is a monofilament, nonabsorbable, sterile, flexible thread prepared from long-chain polyolefin polymer known as polypropylene and is intended for use in soft tissue approximation. The polypropylene surgical suture meets USP requirments as described in the USP Monograph for Nonabsorbable Surgical Sutures; it may be undyed or dyed with an FDA approved color additive; and the suture may be provided with or without a standard needle attached.

Accordingly, FDA has determined that your devices, as approved for marketing under your PMA and PMA supplements, are included in this generic type of device and are, therefore, reclassified into Class II. Although your devices were originally approved under an NDA/PMA application for commercial distribution, you may continue to market your devices subject to the general controls provisions of the Federal Food, Drug, and Cosmetic Act (act) and any performance standards promulgated under section 514 of the act. As such, any new device or any modification to your existing device(s) is subject to the premarket notification provisions of 21 CFR 807.81, and may require a determination of substantial equivalence in order to be marketed.

If you have any questions, please contact Kenneth A. Palmer, Ph.D., at (301) 427-1090.

Sincerely yours,

Robert L. Sheridan
Director
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

Exhibit 41

SECTION 1

MODIFIED DEVICE AND DESCRIPTION

Name of the Device

Modified PROLENE polypropylene mesh

CLASSIFICATION	COMMON NAME	TRADE NAME/ PROPRIETARY NAME
Class II Medical Device, 21 CFR§878.3300	PROLENE polypropylene mesh	PROLENE polypropylene mesh nonabsorbable synthetic surgical mesh

Establishment Registration Number

The ETHICON, Inc. establishment registration number is 2210968.

Device Classification

The FDA has classified PROLENE mesh as a Class II Medical Device under the Division of General and plastic surgery devices (21 CFR§878.3300).

Change or Modification to an Existing Device

Modified PROLENE mesh is a change to an existing preamendment device PROLENE polypropylene mesh nonabsorbable synthetic surgical mesh (see Appendix I for documentation of preamendment status). The modification is to supply additional sizes and a precut key hole shape (see Appendix II). Surgeons routinely cut current product to optimal shapes and prepare a keyhole to accommodate the spermatic cord during the repair of inguinal hernias. Therefore, these changes are intended to provide more convenient shapes and sizes for the same surgical uses.

This is <u>not</u> a Notification for a new device.

Performance Standards

No special controls in the form of performance standards, postmarket surveillance requirements, patient registry requirements have been established for this device. ETHICON, Inc. will comply when any such controls are promulgated.

Continued on next page

MODIFIED DEVICE AND DESCRIPTION, Continued

Physical Description

Modified PROLENE mesh is constructed of knitted filaments of extruded polypropylene identical in composition to that used in PROLENE* polypropylene suture nonabsorbable surgical sutures, U.S.P. (ETHICON, Inc.) The mesh is approximately 0.027 inches thick. This material, when used as a suture, has been reported to be nonreactive and to retain its strength indefinitely in clinical use. The preamendment device, PROLENE mesh, is constructed of the same knitted filaments.

This Notification is to request clearance for labeling changes to add additional sizes and a precut key hole shape .

Modified PROLENE mesh is knitted by a process which interlinks each fiber junction and which provides for elasticity in both directions. This construction permits the mesh to be cut into any shape or size without unraveling. The precut key hole shape is being provided as a convenience to the surgeon. The preamendment predicate device, PROLENE mesh, is made from the same knitting process.

Modified PROLENE mesh is available in single packets as sterile undyed (clear) sheets in seven sizes. The sizes available are 2.5 x 10 cm (1 x 4 inches), 6 x 11cm (2.5 x 4.5 inches), 7.6 x 12.7 cm (3 x 5 inches), 4.5 x 10 cm (1.8 x 4 inches), 6 x 13.7 cm (2.4 x 5.4 inches), 15 x 15 cm (6 x 6 inches), 30 x 30 cm (12 x 12 inches). Each sheet is 0.7 mm (0.027 inch) thick.

Exhibit 42

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

AUG - 9 1996

John D. Paulson, Ph.D.
Vice President, Regulatory Affairs
Ethicon, Inc.
P.O. Box 151
Somerville, New Jersey 08876-0151

Re: K962530
PROLENE Polypropylene Mesh Nonabsorbable Synthetic Surgical Mesh
Regulatory Class: II
Product Code: FTL
Dated: June 25, 1996
Received: June 28, 1996

Dear Dr. Paulson:

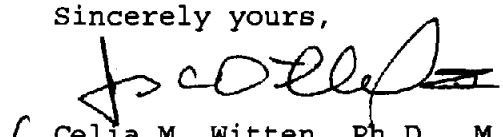
We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Good Manufacturing Practice for Medical Devices: General (GMP) regulation (21 CFR Part 820) and that, through periodic GMP inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4595. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or at (301) 443-6597.

Sincerely yours,



for Celia M. Witten, Ph.D., M.D.
Director
Division of General and
Restorative Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

INDICATION FOR USE

510(k) Number (if known): K962530

Device Name: Modified PROLENE polypropylene mesh nonabsorbable synthetic surgical mesh

Indications for Use: Modified PROLENE polypropylene mesh is indicated for the repair of hernia and other fascial deficiencies that require the addition of a reinforcing or bridging material to obtain the desired surgical result.

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

(Division Sign-Off)
Division of General Restorative Devices
510(k) Number K962530

Prescription Use ✓ OR Over-The Counter Use _____
(Per 21 CFR 801.109)

(Optional Format 1-2-9G)

Exhibit 43

SECTION 1

NEW DEVICE AND DESCRIPTION

Name of the Device

CLASSIFICATION NAME	COMMON NAME	TRADE NAME/ PROPRIETARY NAME
Mesh, Surgical, Polymeric (21CFR, §878.3300)	Pubourethral Sling	To be determined

Establishment Registration Number

The ETHICON, Inc. establishment registration number is #2210968

Manufacturer

This device is distributed by ETHICON, Inc. The device is manufactured by MedScand Medical, P.O. Box 20047, S200 74, Malmo, Sweden.

Device Classification

Surgical mesh is classified by the FDA as a Class II Medical Device, General and Plastic Surgery Devices (21CFR, §878.3300, Product Code 79FTL).

Change or Modification to an Existing Device

The Tension Free Vaginal Tape (TVT) System is a new device, not a modification to an existing device.

Continued on next page

Performance Standards

Mandatory Standards: No special controls in the form of performance standards, postmarket surveillance requirements or patient registry requirements have been established for this device. ETHICON, Inc. will comply with any such controls when promulgated.

Physical Description

The Tension Free Vaginal Tape (TVT) System includes the device and its accessories. The device and accessories are sold separately or as a set. The system consists of the following:

Device:
TVT Device (Sterile, Single-Use)

Accessories (used in conjunction with the device):
TVT Introducer (Non-Sterile, Reusable)
TVT Rigid Catheter Guide (Non-Sterile, Reusable)

TVT Device Description:

The TVT Device is a sterile, single-use device that is composed of polypropylene mesh (also referred here-in as a tape) with approximate dimensions of 0.5 x 16 inches (1.1 x 40cm). This is the same Polypropylene Mesh that is used to fabricate PROLENE polypropylene mesh (K962530). The PROLENE mesh is fabricated from polypropylene strands. These same strands are used to fabricate PROLENE polypropylene Nonabsorbable Surgical Suture (NDA/PMA #16-374) manufactured and marketed by ETHICON, Inc. The mesh is covered with a polyethylene sheath that is cut in the middle across the width (separating the sheath into two pieces). Both the mesh (tape) and sheath are attached at each end to two stainless steel needles by a plastic shrink tubing (collar). The device is used with its dedicated accessories which are described below.

Continued on next page

Physical Description (continued)

Accessories Description:

The TVT Introducer (Accessory) is provided non-sterile for sterilization before surgical use. It is reusable. The introducer is made of stainless steel. It is composed of three (3) parts; 1) handle; 2) threaded staft and 3) rubber O-ring (extra O-rings are provided in the packaged accessory). The metal staft is threaded on one end and notched on the other end for location of the O-ring. The metal staft is contained (inserted) within the handle of the introducer. The introducer functions to facilitate passage of the TVT device from the vagina to abdominal skin.

The TVT Rigid Catheter Guide (Accessory) is provided non-sterile for sterilization before surgical use. It is reusable. The guide is made of stainless steel. The guide is used to add rigidity to the Foley Catheter.

Exhibit 44

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

JAN 28 1998

Mr. Gregory R. Jones
Director, Regulatory Affairs
Ethicon, Inc.
P.O. Box 151
Somerville, New Jersey 08876-0151

Re: K974098
Tension Free Vaginal Tape (TVT) System
Regulatory Class: II
Product Code: FTL
Dated: October 29, 1997
Received: October 30, 1997

Dear Mr. Jones:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the current Good Manufacturing Practice requirement, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic (QS) inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4595. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsmamain.html".

Sincerely yours,

for Celia M. Witten, Ph.D., M.D.
Director
Division of General and
Restorative Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

INDICATION FOR USE

510(k) Number (if known): _____

Device Name: Tension Free Vaginal Tape (TVT) System

Indications for Use: The TVT device is a sterile, single-use device intended to be used as a pubourethral sling indicated for treatment of stress urinary incontinence (SUI), for female urinary incontinence resulting from urethral hypermobility and/or intrinsic sphincter deficiency. The TVT Introducer and Rigid Catheter Guide accessories are intended to facilitate placement of the TVT device. The accessories, available separately, are provided non-sterile and are reusable.

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use X OR Over-The Counter Use _____
(Per 21 CFR 801.109)

(Optional Format 1-2-9G)

(Division Sign-Off)
Division of General Re
510(k) Number K974040

Exhibit 45

SECTION 1

MODIFIED DEVICE AND DESCRIPTION

Name of the Device

CLASSIFICATION NAME	COMMON NAME	TRADE NAME/ PROPRIETARY NAME
Mesh, Surgical, Polymeric (21CFR, §878.3300)	Pubourethral Sling	GYNECARE Tension-Free Vaginal Tape System

Establishment Registration Number

GYNECARE is a Division of ETHICON, Inc a *Johnson and Johnson* Company. The establishment registration number for GYNECARE, a Division of ETHICON, Inc. is #2210968.

Manufacturer

This device is distributed by GYNECARE a Division of ETHICON, Inc., P.O. Box 151, Somerville, NJ 08876-0151. The modified TVT Blue device is manufactured in Neuchatel, Switzerland by ETHICON SarL. The TVT-AA Abdominal Guides and Couplers are manufactured in the USA by GYNEACRE a Division of ETHICON, Inc., Somerville, NJ.

Device Classification

Surgical mesh is classified by the FDA as a Class II Medical Device, General and Plastic Surgery Devices (21CFR, §878.3300, Product Code 79FTL).

Predicate Device(s)

TVT-blue is a modification of the currently marketed TVT device and accessories covered under 510(k) K974098 cleared January 28, 1998. It contains the same blue pigmented polypropylene monofilaments as the currently cleared PROLENE* SOFT Polypropylene Mesh K001122 cleared on May 23, 2000.

Continued on next page

* Trademark

MODIFIED DEVICE AND DESCRIPTION, Continued

Predicate Device Continued

The predicate device for the accessory TVT-AA abdominal guides is the Stamey Needle manufactured by COOK OB/GYN, K884553, cleared November 14, 1988. Other similar predicate devices include various Stamey Needles manufactured by Cook OB/GYN as well as the Raz and Pereyra.

Change or Modification to an Existing Device

The modified TVT Blue System is a modification to the existing Tension Free Vaginal System (TVT) system herein referred to as the TVT System. TVT-Blue is distinguished by the inclusion of blue pigmented polypropylene fibers (approximately 50%) interwoven in the same manner as the current unpigmented TVT device. The blue pigmented monofilaments are made from the same unpigmented polypropylene fibers colored with blue pigment [Phthalocyaninato(2-)] copper. The Color Index Number is 74160 as referenced in 21CFR § 74.3045. This is the same color additive used in PROLENE* Polypropylene Suture. The purpose of the blue monofilaments is to offer greater visibility of the TVT mesh as it is placed along the midurethra.

TVT-AA is an accessory to the TVT system. TVT-AA will be available as an accessory to the unpigmented predicate TVT device and to the modified TVT blue device. TVT-AA consists of two disposable abdominal guides and two disposable couplers to facilitate the placement of the TVT mesh using an abdominal approach. TVT is currently placed transvaginally. The abdominal guides and couplers allow Urologists, who are more comfortable with an abdominal approach as a result of their training, to apply TVT mesh using an abdominal approach versus a transvaginal approach. The placement of the TVT mesh is unchanged as it is placed on the midurethra. This is not a new device only an alternative approach to accessing the vagina for placement of TVT mesh.

Continued on next page

MODIFIED DEVICE AND DESCRIPTION, Continued

Performance Standards

No special controls in the form of performance standards, postmarket surveillance requirements or patient registry requirements have been established for this device. GYNECARE a Division of ETHICON, Inc. will comply with any such controls when promulgated.

Physical Description

The current Tension Free Vaginal Tape (TVT) System currently includes the device and its accessories. The device and accessories are sold separately or as a set. The system consists of the following:

Device: TVT Device (Sterile, Single-Use)
Accessories (used in conjunction with the device):
TVT Introducer (Non-Sterile, Reusable)
TVT Rigid Catheter Guide (Non-Sterile, Reusable)
TVT Abdominal Guides and Couplers provided sterile (packaged with TVT Single-Use Device)

TVT- Blue System Description:

The TVT blue device is a sterile, single-use device that is composed of one piece of approximately 50% unpigmented and 50% pigmented blue [(Phthalocyaninato(2-) copper], Colour index. Number 74160) polypropylene mesh (referred here-in as a tape) with approximate dimensions of 0.5 x 16 inches (1.1 x 40cm). This is the same Polypropylene Mesh that is used to fabricate PROLENE* Soft Polypropylene mesh (K001122) and PROLENE* Polypropylene Mesh (K962530). The PROLENE mesh is fabricated from polypropylene strands of clear and clear/blue pigmented polypropylene fiber. The blue pigmented polypropylene monofilaments comprise approximately 50% of the mesh. These same strands are used to fabricate PROLENE* Polypropylene Nonabsorbable Surgical Suture, undyed of blue pigment, (NDA/PMA #16-374) manufactured and marketed by ETHICON, Inc. The mesh is covered with a polyethylene sheath that is cut in

Continued on next page

MODIFIED DEVICE AND DESCRIPTION, Continued

Physical Description Continued

the middle across the width (separating the sheath into two pieces). Both the mesh (tape) and sheath are attached at each end to two stainless steel needles by a plastic shrink tubing (collar). The device is used with its dedicated accessories, TVT Introducer and Rigid Catheter Guide, and may be used with the TVT-AA accessory to facilitate an abdominal approach as described below.

TVT-AA Accessory Description:

The TVT-AA consists of two disposable stainless steel abdominal guides and two disposable polypropylene couplers. It is provided sterile. The tip of the abdominal guide is designed to accept the smaller, tapered end of the coupler with a press fit, while the distal, or wider end is designed to accept the current TVT needle with a press fit. The abdominal guides allow Urologists, who are already more familiar with an abdominal approach, to pass the guides from an abdominal insertion out through the vagina. The couplers are attached to the TVT needle and then attached to the abdominal guide. The TVT needle, and tape are then passed back up the vagina toward the abdomen (current procedure) following the path of the guide. The TVT needle is pushed from below, per the current instructions for use and the guide is used to simply "guide the interlocked unit out through the abdomen. The abdominal approach does not change the intended use of the TVT, unpigmented or blue mesh, but simply offers a choice of an abdominal approach or a transvaginal approach to TVT, sling repair.

Exhibit 46

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

OCT 2 6 2001

Gregory R. Jones
Director of Regulatory Affairs
and Quality Assurance
Gynecare
Division of Ethicon , Inc.
P.O. Box 151
Somerville, New Jersey 08876

Re: K012628
Trade/Device Name: GYNECARE Tension-Free Vaginal Tape (TVT) Blue System
Regulation Number: 878.3300
Regulation Name: Surgical Mesh
Regulatory Class: II
Product Code: FTL
Dated: August 9, 2001
Received: August 13, 2001

Dear Mr. Jones:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set

forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 21 CFR Part 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4659. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/dsma/dsmamain.html

Sincerely yours,

Susan Walker, MS

Celia M. Witten, Ph.D., M.D.
Director
Division of General, Restorative
and Neurological Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

INDICATION FOR USE

510(k) Number (if known): K012628

Device Name: Tension Free Vaginal Tape (TVT) Blue System

Indications for Use:

The TVT device is intended to be used as a pubourethral sling indicated for treatment of stress urinary incontinence (SUI) for female urinary incontinence resulting from urethral hypermobility and/or intrinsic sphincter deficiency. The TVT Introducer, Rigid Catheter Guide and TVT Abdominal Guides and Couplers are accessories intended to facilitate placement of the TVT device.

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ✓ OR Over-The Counter Use _____
(Per 21 CFR 801.109)

(Division Sign-Off)
Division of General, Restorative and Neurological Devices

(Optional Format 1-2-9G)

Exhibit 47

SECTION 1

MODIFIED DEVICE AND DESCRIPTION

Name of the Device

CLASSIFICATION NAME	COMMON NAME	TRADE NAME/ PROPRIETARY NAME
Mesh, Surgical, Polymeric (21CFR, §878.3300)	Pubo-urethral Sling	GYNECARE TVT Obturator System

Establishment Registration Number

GYNECARE is a Division of ETHICON, Inc a *Johnson and Johnson* Company. The establishment registration number for GYNECARE, a Division of ETHICON, Inc. is #2210968.

Device Classification

Surgical mesh is classified by the FDA as a Class II Medical Device, General and Plastic Surgery Devices (21CFR, §878.3300, Product Code 79FTL).

Predicate Device(s)

The fundamental scientific technology of the GYNECARE TVT Obturator device is unchanged from the predicate device. GYNECARE TVT Obturator device is a modification of the currently marketed GYNECARE TVT device covered under 510(k) K974098 cleared January 28, 1998. It contains the same blue pigmented polypropylene monofilaments as the currently cleared TVT Blue with Abdominal Guides K012628 cleared on October 26, 2001.

The predicate device for the accessories; Helical Passers and Winged Guide is the GYNECARE TVT AA Abdominal Guides covered under 510(k) K012628 cleared on October 26, 2001. Another similar predicate device is the American Medical Systems' MONARC™ Subfacial Hammock Helical Needles covered under 510(k) K02356 cleared on November 19, 2002.

Change or Modification to an Existing Device	GYNECARE TVT Obturator System maintains the same fundamental scientific technology as the predicate device. The primary change to the device is the replacement of the needles with plastic tube receptacles to accommodate the accessory; Helical Passer (provided assembled for convenience). The PROLENE mesh implant and plastic sheath remain unchanged. Two accessories are provided with the GYNECARE TVT Obturator device; 1) GYNECARE Helical Passer, 2) GYNECARE Winged Guide. The Helical Passer and Winged guide are provided to facilitate placement of the TVT Obturator device. For comparison, photos of the modified and predicate device are included in Attachment III. The GYNECARE TVT Obturator device will be primary packaged together with Helical Passers and Winged Guide in a plastic tray (workstation) placed within a plastic 'tub'with a tyvek label that serves as the sterility barrier, and placed in a labeled carton.
Physical Description	GYNECARE TVT Obturator System includes the device and its accessories. The device and accessories are sold as a set. The system consists of the following: Device: GYNECARE TVT Obturator device (Sterile, Single-Use) Accessories (used in conjunction with the device): GYNECARE TVT Helical Passers (Sterile, Single Use) GYNECARE TVT Winged Guide (Sterile, Single Use) *Physical Description Continued on Next Page*

GYNECARE TVT Obturator device:

The GYNECARE TVT *Obturator* device is a sterile, single patient use device, consisting of one piece of undyed or blue (Phtalocyanine blue, Color index Number 74160) PROLENE* polypropylene mesh (tape) covered by a plastic sheath overlapping in the middle. Medical grade plastic tube receptacles are attached at each end of the mesh to accommodate the Helical Passers. The Helical Passers come assembled to the GYNECARE TVT Obturator device and are used to deliver of the mesh implant via the trans-obturator "inside-out" approach. The "inside-out" approach delivers the mesh trans-vaginally, along the posterior ischiopubic ramus and through the obturator membrane.

GYNECARE TVT Helical Passers:

The GYNECARE TVT Helical Passers are two stainless steel, curved wire passers with plastic handles and are designed to deliver the GYNECARE TVT *Obturator* device. Helical Passers are provided as left and right units, pre-assembled to the GYNECARE TVT Obturator device.

GYNECARE TVT Winged Guide

The GYNECARE TVT Winged Guide is a stainless steel accessory instrument, which facilitates the passage of the GYNECARE TVT Helical Passers through the dissection tract. This accessory is offered as an adjunct to the device.

Exhibit 48

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

DEC - 8 2003

Mr. Sean O'Bryan
Senior Project Manager, Regulatory Affairs
Ethicon, Inc.
Route 22 West
Somerville, New Jersey 08876

Re: K033568
Trade/Device Name: GYNECARE TVT Obturator Device
Regulation Number: 21 CFR 878.3300
Regulation Name: Surgical mesh
Regulatory Class: II
Product Code: FTL
Dated: November 10, 2003
Received: November 13, 2003

Dear Mr. O'Bryan:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of Compliance at (301) 594-4659. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/dsma/dsmamain.html

Sincerely yours,

Miriam C. Provost

for Celia M. Witten, Ph.D., M.D.
Director
Division of General, Restorative
and Neurological Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

INDICATION FOR USE

510(k) Number (if known): K033568

Device Name: **GYNECARE TVT Obturator device**

Indications for Use: The GYNECARE TVT *Obturator* device is intended for use in women as a sub-urethral sling for the treatment of stress urinary incontinence (SUI) resulting from urethral hypermobility and/or intrinsic sphincter deficiency.

Miriam C. Provost
(Division Sign-Off)
Division of General, Restorative
and Neurological Devices

510(k) Number K033568

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use X OR Over-The Counter Use _____
(Per 21 CFR 801.109)

(Optional Format 1-2-9G)

Exhibit 49

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Room –WO66-G609
Silver Spring, MD 20993-0002

Mr. Gregory R. Jones
Director, Regulatory Affairs
Ethicon, Inc.
P.O. Box 151
SOMERVILLE NJ 08876

SEP 28 2012

Re: K974098
Trade/Device Name: Tension Free Vaginal Tape (TVT) System
Regulation Number: 21 CFR 878.3300
Regulation Name: Surgical mesh
Regulatory Class: II
Product Code: OTN
Dated: October 29, 1997
Received: October 30, 1997

Dear Mr. Jones:

This letter corrects our substantially equivalent letter of January 28, 1998.

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

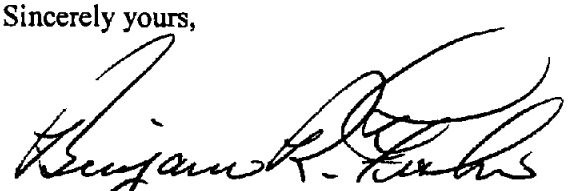
Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must

comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please go to http://www.fda.gov/AboutFDA/CentersOffices/CDRH/CDRHOffices/ucm115809.htm for the Center for Devices and Radiological Health's (CDRH's) Office of Compliance. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,



Benjamin R. Fisher, Ph.D.
Director
Division of Reproductive, Gastro-Renal,
and Urological Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

INDICATION FOR USE

510(k) Number (if known): _____

Device Name: Tension Free Vaginal Tape (TVT) System

Indications for Use: The TVT device is a sterile, single-use device intended to be used as a pubourethral sling indicated for treatment of stress urinary incontinence (SUI), for female urinary incontinence resulting from urethral hypermobility and/or intrinsic sphincter deficiency. The TVT Introducer and Rigid Catheter Guide accessories are intended to facilitate placement of the TVT device. The accessories, available separately, are provided non-sterile and are reusable.

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use X OR Over-The Counter Use _____
(Per 21 CFR 801.109)

(Optional Format 1-2-9G)

(Division Sign-Off)
Division of Cardiovascular, Respiratory, and Neurological Devices
510(k) Number K974040

Tension Free Vaginal Tape (TVT) System
ETHICON, Inc.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-002

September 28, 2012

Dear Manufacturer:

In 2010, the Division of Reproductive, Gastro-Renal, and Urological Devices (DRGUD) in the Office of Device Evaluation (ODE) in the Center for Devices and Radiological Health (CDRH) took over lead review responsibility of surgical mesh indicated pelvic organ prolapse and stress urinary incontinence from the Division of Surgical, Orthopedic, and Restorative Devices (DSORD).

DRGUD has developed new product codes for surgical mesh indicated for pelvic organ prolapse and stress urinary incontinence and is issuing corrected substantial equivalence letters to manufacturers of these devices to reflect the new product codes. The following table lists the new product codes and their respective descriptions.

Product Code	Product Code Description
OTM	mesh, surgical, for stress urinary incontinence, male
OTN	mesh, surgical, **synthetic**, urogynecologic, for stress urinary incontinence, female, **multi-incision**
PAG	mesh, surgical, **non-synthetic**, urogynecologic, for stress urinary incontinence, female, **multi-incision**
PAH	mesh, surgical, **synthetic**, urogynecologic, for stress urinary incontinence, female, **single-incision mini-sling**
OTO	mesh, surgical, **synthetic**, urogynecologic, for apical vaginal and uterine prolapse, **transabdominally placed**
PAJ	mesh, surgical, **non-synthetic**, urogynecologic, for apical vaginal and uterine prolapse, **transabdominally placed**
OTP	mesh, surgical, **synthetic**, urogynecologic, for pelvic organ prolapse, **transvaginally placed**
PAI	mesh, surgical, **non-synthetic**, urogynecologic, for pelvic organ prolapse, **transvaginally placed**

Please note that the regulatory class (Class II) and the regulation number (21 CFR 878.3300) for surgical mesh indicated for pelvic organ prolapse and stress urinary incontinence remains unchanged at this time.

If you have any questions regarding the contents of this letter, please contact Sharon Andrews at (301) 796-6529 or Rebecca Robinson, Ph.D., at (301) 796-6532.

Sincerely yours,

Benjamin R. Fisher, Ph.D.
Director
Division of Reproductive, Gastro-Renal,
and Urological Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Exhibit 50

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Room –WO66-G609
Silver Spring, MD 20993-0002

Mr. Gregory R. Jones
Director of Regulatory Affairs and Quality Assurance
Gynecare
Division of Ethicon
P.O. Box 151
SOMERVILLE NJ 08876

SEP 28 2012

Re: K012628
Trade/Device Name: GYNECARE Tension-Free Vaginal Tape (TVT) Blue System
Regulation Number: 21 CFR 878.3300
Regulation Name: Surgical mesh
Regulatory Class: II
Product Code: OTN
Dated: August 9, 2001
Received: August 13, 2001

Dear Mr. Jones:

This letter corrects our substantially equivalent letter of October 26, 2001.

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

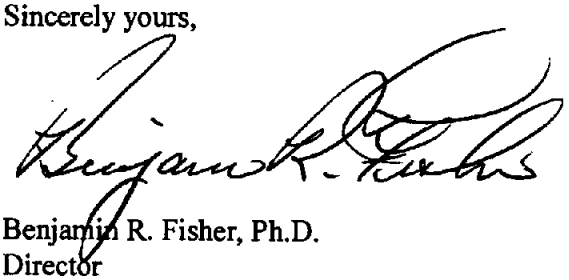
Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must

comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please go to http://www.fda.gov/AboutFDA/CentersOffices/CDRH/CDRHOffices/ucm115809.htm for the Center for Devices and Radiological Health's (CDRH's) Office of Compliance. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,



Benjamin R. Fisher, Ph.D.
Director
Division of Reproductive, Gastro-Renal,
and Urological Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

INDICATION FOR USE

510(k) Number (if known): K012628

Device Name: Tension Free Vaginal Tape (TVT) Blue System

Indications for Use: The TVT device is intended to be used as a pubourethral sling indicated for treatment of stress urinary incontinence (SUI) for female urinary incontinence resulting from urethral hypermobility and/or intrinsic sphincter deficiency. The TVT Introducer, Rigid Catheter Guide and TVT Abdominal Guides and Couplers are accessories intended to facilitate placement of the TVT device.

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ✓ (Per 21 CFR 801.109) OR Over-The Counter Use _____

(Division Sign-Off) (~~Optional~~ Format 1-2-9G)
Division of General, Restorative and Neurological Devices

Modified TVT Blue and TVT-AA 510(k) Number K012628

Exhibit 51

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Room - WO66-G609
Silver Spring, MD 20993-0002

SEP 28 2012

Mr. Sean O'Bryan
Senior Project Manager, Regulatory Affairs
Ethicon, Inc.
Route 22 West
SOMERVILLE NJ 08876

Re: K033568
Trade/Device Name: GYNECARE TVT Obturator Device
Regulation Number: 21 CFR 878.3300
Regulation Name: Surgical mesh
Regulatory Class: II
Product Code: OTN
Dated: November 10, 2003
Received: November 13, 2003

Dear Mr. O'Bryan:

This letter corrects our substantially equivalent letter of December 8, 2003.

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

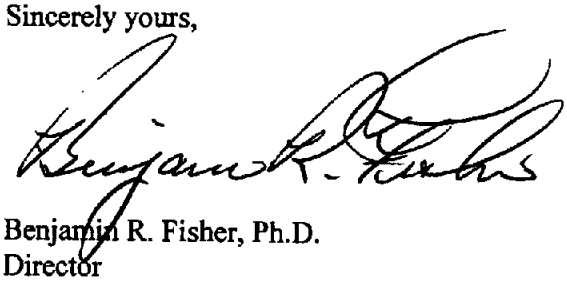
Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must

comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please go to http://www.fda.gov/AboutFDA/CentersOffices/CDRH/CDRHOffices/ucm115809.htm for the Center for Devices and Radiological Health's (CDRH's) Office of Compliance. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,



Benjamin R. Fisher, Ph.D.
Director
Division of Reproductive, Gastro-Renal,
and Urological Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

INDICATION FOR USE

510(k) Number (if known): K033568

Device Name: **GYNECARE TVT Obturator device**

Indications for Use: The GYNECARE TVT *Obturator* device is intended for use in women as a sub-urethral sling for the treatment of stress urinary incontinence (SUI) resulting from urethral hypermobility and/or intrinsic sphincter deficiency.

Miriam C. Provost
(Division Sign-Off)
Division of General, Restorative
and Neurological Devices

510(k) Number K033568

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use X OR Over-The Counter Use _____
(Per 21 CFR 801.109)

(Optional Format 1-2-9G)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-002

September 28, 2012

Dear Manufacturer:

In 2010, the Division of Reproductive, Gastro-Renal, and Urological Devices (DRGUD) in the Office of Device Evaluation (ODE) in the Center for Devices and Radiological Health (CDRH) took over lead review responsibility of surgical mesh indicated pelvic organ prolapse and stress urinary incontinence from the Division of Surgical, Orthopedic, and Restorative Devices (DSORD).

DRGUD has developed new product codes for surgical mesh indicated for pelvic organ prolapse and stress urinary incontinence and is issuing corrected substantial equivalence letters to manufacturers of these devices to reflect the new product codes. The following table lists the new product codes and their respective descriptions.

Product Code	Product Code Description
OTM	mesh, surgical, for stress urinary incontinence, male
OTN	mesh, surgical, **synthetic**, urogynecologic, for stress urinary incontinence, female, **multi-incision**
PAG	mesh, surgical, **non-synthetic**, urogynecologic, for stress urinary incontinence, female, **multi-incision**
PAH	mesh, surgical, **synthetic**, urogynecologic, for stress urinary incontinence, female, **single-incision mini-sling**
OTO	mesh, surgical, **synthetic**, urogynecologic, for apical vaginal and uterine prolapse, **transabdominally placed**
PAJ	mesh, surgical, **non-synthetic**, urogynecologic, for apical vaginal and uterine prolapse, **transabdominally placed**
OTP	mesh, surgical, **synthetic**, urogynecologic, for pelvic organ prolapse, **transvaginally placed**
PAI	mesh, surgical, **non-synthetic**, urogynecologic, for pelvic organ prolapse, **transvaginally placed**

Please note that the regulatory class (Class II) and the regulation number (21 CFR 878.3300) for surgical mesh indicated for pelvic organ prolapse and stress urinary incontinence remains unchanged at this time.

If you have any questions regarding the contents of this letter, please contact Sharon Andrews at (301) 796-6529 or Rebecca Robinson, Ph.D., at (301) 796-6532.

Sincerely yours,

Benjamin R. Fisher, Ph.D.
Director
Division of Reproductive, Gastro-Renal,
and Urological Devices
Office of Device Evaluation
Center for Devices and Radiological Health